NLC
NUTRICIA LEARNING CENTER

Inflammation in Chronic Kidney Disease (CKD)

Vishal Bagchi, MBA RD LD

October 12, 2022

1

Disclosure

- Vishal Bagchi is employed by Nutricia North America
- Slides are scientific and based on information and research evidence available during the time of the lecture
- Non-biased and Non-Promotional

No conflict of interest for this presentation

2

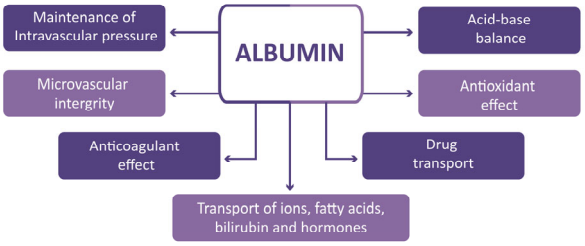
Objectives

- Participants will be able to
  - Discuss the markers of inflammation in CKD
  - Identify causes of inflammation in CKD
  - Discuss current recommendations for management of inflammation in CKD

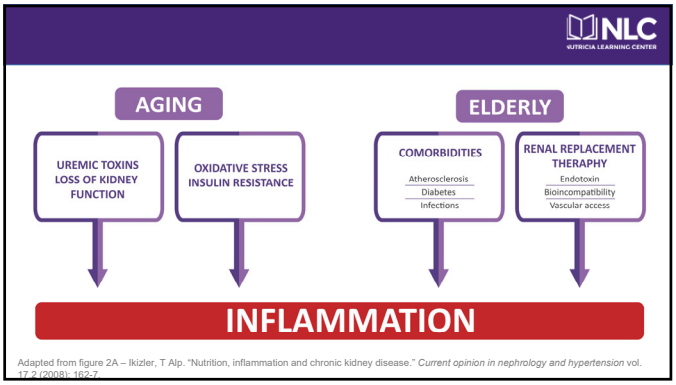
3

Importance of albumin

PHYSIOLOGICAL EFFECTS OF EXOGENOUS ALBUMIN



4



Adapted from figure 2A – Ikizler, T Alp. "Nutrition, inflammation and chronic kidney disease." *Current opinion in nephrology and hypertension* vol. 17.2 (2008): 162-7.

5

Malnutrition-Inflammation Complex Syndrome (MICS)

- Protein-energy malnutrition and inflammation that occur concurrently and coexist in individuals with CKD
- Malnutrition-inflammation-atherosclerosis syndrome (MIA) is also used to describe the combination of malnutrition, inflammation and atherosclerosis
- Changes in acute-phase serum proteins
- Hypercatabolic state
- Diminished appetite/anorexia
- Erythropoietin hyporesponse

Yamada, Shunsuke et al. "Emerging cross-talks between chronic kidney disease-mineral and bone disorder (CKD-MBD) and malnutrition-inflammation complex syndrome (MICS) in patients receiving dialysis." Clinical and experimental nephrology vol. 26,7 (2022): 613-629. doi:10.1007/s10157-022-02216-x

6

Acute-phase protein

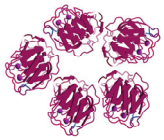
- "Positive" acute-phase proteins:
  - C-reactive protein
  - Ferritin and others
- "Negative" acute-phase proteins
  - Decreases during inflammation
  - Albumin
  - Transferrin and others
  - Physiological role of decreased synthesis of such proteins is generally to save **amino acids** for producing "positive" acute-phase proteins more efficiently.

7

Role of C-reactive protein in CKD

- Acute phase reactant
- Rises during inflammatory processes
- Early defense against infections
- Secreted in liver
- Associated with low Hgb and/ or EPO resistance
- CRP was an independent predictor for higher all-cause mortality and increased risk of developing major adverse cardiovascular events
- Serum C-reactive protein to albumin ratio(CAR) ↑ all-cause mortality in PD.

- Normal: Less than 10 mg/L
- High: Equal to or greater than 10 mg/L



Liu, Siyi et al. "Serum C-reactive protein to albumin ratio and mortality associated with peritoneal dialysis." Renal failure vol. 42,1 (2020): 600-606. doi:10.1080/0886022X.2020.1783680

8

CRP elevated in peritoneal dialysis (PD)

- Studies have shown an inverse relationship between serum albumin and CRP levels in hemodialysis patients.
- CRP has been found to be elevated in PD patients with chronic infection
- CRP values become significant elevated during peritonitis
- Poor adequacy increases inflammation

Valga, Francisco et al. "Inflammation and hemodialysis adequacy: Are C-reactive ¿están los niveles de proteína C reactiva influidos por la dosis de diálisis recibida?." Nefrologia, S0211-6995(21)00112-0. 5 Jul. 2021.
Cueto-Manzano, Alfonso M et al. "Systemic inflammation May limit the effect of protein supplement on nutritional status in peritoneal dialysis." *Clinical nutrition ESPEN* vol. 49 (2022): 307-313.

9

CRP in peritoneal dialysis

- 34 malnourished patients(SGA)
- 6 months nutrition counselling + protein supplements (Egg albumin)
- Two groups based on C-reactive protein (hsCRP)
  - Inflammation (>3 mg/L)
    - 70% improved, 25% no change and 5% worsened
    - Albumin 3.0 →3.4 (g/dL)
    - BMI 20.3 →21.6 kg/m2
  - No-inflammation (≤3 mg/L)
    - 50% improved, 36% no change and 14% worsened
    - Albumin 2.8 →3.0 g/dL
    - 21.9 ± 3.0 vs 22.5 kg/m2

Cueto-Manzano AM, et al. Systemic inflammation May limit the effect of protein supplement on nutritional status in peritoneal dialysis. *Clin Nutr ESPEN*. 2022;49:307-313.

10

CRP

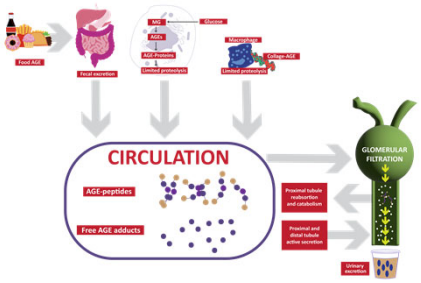
- 50% of pts with a GFR 15-60 have a CRP>2.1mg/L
- Europe – median CRP for dialysis 5mg/L
- Americans – slightly higher (~6.8)
- Asians – substantially lower
- Why isn't it used more?
  - Cheap
  - Reliable
  - No trials to show usefulness (dialysis setting)
- Higher in Covid-19 patients

Romão JE Jr, et al. Positive acute-phase inflammatory markers in different stages of chronic kidney disease. *Am J Nephrol*. 2006;26(1):59-66.

11

Advanced Glycation End Products (AGE)

- Compounds produced when sugars combine with proteins, fats and other ingredients in food (Maillard, 1912)
- Increase oxidation and inflammation
- AGE's can modify LDL cholesterol to make it easier to oxidize and easier to deposit in blood vessels
- The older you get the harder it is for your body to get rid of AGEs
- Kidneys clear AGE



Sergi D, Boulestin H, Campbell FM, Williams LM. The Role of Dietary Advanced Glycation End Products in Metabolic Dysfunction. Mol Nutr Food Res. 2021;65(1):e1900934.

12

Role of diet and AGE levels

Restriction of AGE in diet to prevent DM, CKD and atherosclerosis is **extrapolated.**

- Cross sectional with 2-year F/U of healthy adults and CKD-3 patients
- 325 healthy adults and 66 CKD-3 patients
- Diet modifications
- Results:
  - Reducing dietary AGE intake significantly decreases oxidative stress in both healthy participants and CKD-3

Vlassara H, et al. Protection against loss of innate defenses in adulthood by low advanced glycation end products (AGE) intake: role of the anti-inflammatory AGE receptor-1. *J Clin Endocrinol Metab.* 2009;94(11):4483-4491

13

AGE content of foods

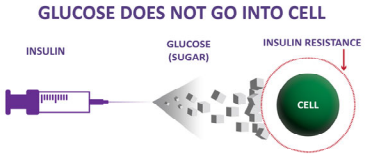
- Poached or steamed chicken had half the AGE of roasted or broiled
- Scrambled eggs prepared with cooking spray, margarine or oil had ~50% to 75% less AGE than if cooked with butter

Uribarri, Jaime et al. "Advanced glycation end products in foods and a practical guide to their reduction in the diet." *Journal of the American Dietetic Association* vol. 110,6 (2010): 911-16.

14

AGE and insulin resistance

- NHANES III – found that GFR was lower in pts who were insulin resistant
- Which came first? Insulin resistance or inflammation?



Foley RN, Wang C, Ishani A, Collins AJ. NHANES III: influence of race on GFR thresholds and detection of metabolic abnormalities. *J Am Soc Nephrol.* 2007;18(9):2575-2582. doi:10.1681/ASN.2006121411

15

Role of diet in AGE

- Found naturally in animal-derived foods before cooking
- Cooking forms new AGEs in these foods

Uribarri J, Woodruff S, Goodman S, Cai W, Chen X, Pyzik R, Yong A, Striker GE, Vlassara H. Advanced glycation end products in foods and a practical guide to their reduction in the diet. J Am Diet Assoc 2010;110:911–6.

16

The take home on AGE

- AGEs play an indirect role in CKD and its progression
- Reducing exposure to AGEs may become an important disease prevention strategy
- The message: eat more whole foods, avoid processed foods, increase fruits and vegetables

Avoid frying, grilling, roasting and broiling!

Use boiling, poaching, steaming or stewing

17

Abdominal obesity

- More fat = more inflammation
- More muscle = less inflammation
- Associated higher prevalence of malnutrition and inflammation
- Lower muscle mass and strength
- Waist circumference better indicator vs. BMI

Brooks GC, Blaha MJ, Blumenthal RS. Relation of C-reactive protein to abdominal adiposity. Am J Cardiol. 2010;106(1):56–61

18

The advent of discussions about nitrogen balance

- Borah et al – study on nitrogen balance(1978)
  - High (1.44 g/kg/d) and low protein diets (0.5 g/kg/d)
  - Low, always negative nitrogen balance
  - High in negative nitrogen balance on dialysis days only
- The process of dialysis increases CRP and IL-6
  - Inflammatory acute phase reactants markers

Borah MF, et al. Nitrogen balance during intermittent dialysis therapy of uremia. *Kidney Int.* 1978;14(5):491-500.

19

That is a LOT of protein

90 kg Male eating 1.44 g protein/kg BW/d
= 130 g protein/d
= 6 3-oz servings of steak
= 9 1-fl oz of a LQ Protein

=

Recommendation for PD:
1.2-1.3 g protein/kg/BW/d
= 108 g protein/d
= 5 3-oz servings of steak
= 7 1-fl oz of a LQ Protein

=

20

Hemodialysis

- Hemodialysis is associated with the activation of an "inflammatory cascade"
  - Exposure of blood to dialysis membranes
  - Less than sterile dialysate
  - Ultra pure dialysate has shown improvements in inflammatory markers, response to EPO and slower loss of residual renal function

Cao H, Ye H, Sun Z. Et al., Circulatory mitochondrial DNA is a pro-inflammatory agent in maintenance hemodialysis patients. PloS One. 2014;9(12):e113179

21

Peritoneal dialysis

- Protein loss in dialysate
- Feeling of fullness due to PD Fluids
- Protein energy wasting

Studart MMMQ, Furioso ACT, Veiga JPR, Rodrigues ME, Gomes LO, Moraes CF. Impact of different automated peritoneal dialysis modalities on the inflammatory profile of elderly patients with chronic kidney disease [published online ahead of print, 2022 Jun 13]. J Bras Nefrol. 2022;S0101-28002022005032401.

22

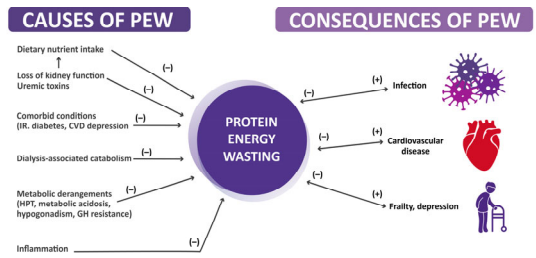
Does the dialysis solution play a role in inflammation?

- Glucose Degradation Products (GDP) in dialysate lead to inflammation and then fibrosis
- GDP's in the dialysis solution and the reactive carbonyl compounds in uremia lead to AGE
- Authors suggest adequate nutrition support and screening for "persistent inflammation"

Lai KN, Leung JC. Inflammation in peritoneal dialysis. *Nephron Clin Pract*. 2010;116(1):c11-c18

23

Protein Energy Wasting



Based on: Ikizler TA, et al. Prevention and treatment of protein energy wasting in chronic kidney disease patients: a consensus statement by the International Society of Renal Nutrition and Metabolism. *Kidney Int*. 2013;84(6):1096-1107

24

Protein Energy Wasting (PEW) is common in CKD

- PEW is found in 20-50% of patients with advanced kidney disease
- PEW sharply increases mortality risk and frequency of hospitalizations
- One study found that in the first 48 hours of hospitalization pts met only 7% of protein needs and 14% of calorie needs

Ikizler TA, et al. Prevention and treatment of protein energy wasting in chronic kidney disease patients: a consensus statement by the International Society of Renal Nutrition and Metabolism. *Kidney Int.* 2013;84(6):1096-1107

25

How does inflammation effect appetite?

26

Anorexia

- A metabolic effect of inflammation
- Animal studies have shown that cytokines have a direct effect on the satiety center
- Animal studies have also shown an increase in skeletal muscle breakdown in response to TNF-α administration
- Diminished appetite (anorexia) is associated with higher concentration of proinflammatory cytokines, higher levels of EPO hyporesponisveness and poor clinical outcome.

Icardi A, Paoletti E, De Nicola L, Mazzaferro S, Russo R, Cozzolino M. Renal anaemia and EPO hyporesponsiveness associated with vitamin D deficiency: the potential role of inflammation. Nephrol Dial Transplant. 2013 Jul;28(7):1672–9.

27

Anemia and nutritional status

- Improving nutritional state in dialysis patients may also improve anemia and lead to lower required EPO dose.
- 2019 González-Ortiz et al, 61 HD PEW is an incremental predictor of poor responsiveness to EPO in HD patients

González-Ortiz, Allema et al. "Relationship between protein-energy wasting in adults with chronic hemodialysis and the response to treatment with erythropoietin." *BMC nephrology* vol. 20,1 316. 14 Aug. 2019, doi:10.1186/s12882-019-1457-0

28

Albumin management and ESA use

- There is an inverse relationship between ESA dose and appetite
  - Locatelli F, et al. Nutritional-inflammation status and resistance to erythropoietin therapy in haemodialysis patients. *Nephrol Dial Transplant*. 2006;21(4):991-998
- Increase in serum albumin concentration is associated with rapid improvement in anemia. Such a rate of anemia correction can only be realized by tripling the dose of ESAs
  - Agarwal R, Davis JL, Smith L. Serum albumin is strongly associated with erythropoietin sensitivity in hemodialysis patients. *Clin J Am Soc Nephrol*. 2008;3(1):98-104

29

How do RD's effect EPO usage?

- Better nutrition status = better EPO responsiveness
- Our responsibility for addressing inflammation

30

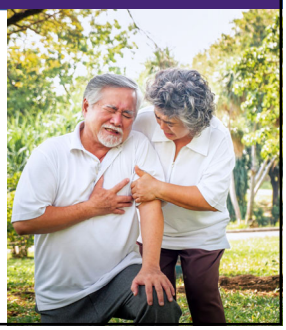
Hidden inflammation

- Dental inflammation
- Bed sores
- Foot sores
- Uncontrolled diabetes
- Lack of exercise
- Stress

31

What do CKD patients die of?

- Cardiovascular mortality
- Uremic dyslipidemia
- Infection
- Malnutrition and failure to thrive



32

What can be done to reduce inflammation and increase qol?

- Vitamin D
- Omega's
- Exercise
- Diet counseling
- Enteral nutrition

33

Vitamin D

- Starts decreasing in Stage III
- In Stage VI the median is 15-20 ng/ml
- Vitamin D is an acute phase reactant – levels decrease with inflammation
- Which came first?
  - Inflammation = low Vit D
  - Low vit D = Inflammation

Waldron, Jenna Louise et al. "Vitamin D: a negative acute phase reactant." *Journal of clinical pathology* vol. 66,7 (2013): 620-2. doi:10.1136/jclinpath-2012-201301

34

Oral cholecalciferol in dialysis patients with vitamin D deficiency

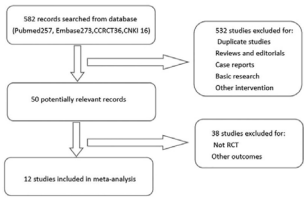
- 56 patients' baseline $25OHD_3$ level <20 ng/mL
- 100 IU of cholecalciferol per kg body weight once weekly orally for 26 weeks
- $25OHD_3$ 9.9 →26.1 ng/mL
- Cinacalcet therapy was positively associated
- iPTH level significantly decreased from median 362 pg/mL to 297 pg/mL

Zitt, Emanuel et al. "Efficacy and safety of body weight-adapted oral cholecalciferol substitution in dialysis patients with vitamin D deficiency." BMC nephrology vol. 16 128. 4 Aug. 2015, doi:10.1186/s12882-015-0116-3

35

Omega-3 A meta-analysis, Hu et. al 2017

- Inflammatory biomarkers
  - C-reactive protein (CRP),
  - interleukin-6 (IL-6)
  - tumor necrosis factor-α (TNF-α)
- Insufficient evidence



Hu, Chun et al. "Effects of Omega-3 Fatty Acids on Markers of Inflammation in Patients With Chronic Kidney Disease: A Controversial Issue." Therapeutic apheresis and dialysis : official peer-reviewed journal of the International Society for Apheresis, the Japanese Society for Apheresis, the Japanese Society for Dialysis Therapy vol. 22,2 (2018): 124-132. doi:10.1111/1744-9987.12611

36

Dietary Omega-3 vs Omega-6

- Mortality in long-term hemodialysis patients is high, mostly attributed to cardiovascular events, and may be related to chronic inflammation. We hypothesized that the anti-inflammatory benefits of higher dietary intake of omega-3 compared with omega-6 polyunsaturated fatty acids may modulate the inflammatory processes and decrease death risk.
- 145 hemodialysis patients from 8 DaVita dialysis clinics in Southern California in 2001-2007.
- Intake of dietary omega-3 and ratio of omega-6 to omega-3 using 3-day food record supplemented by dietary interview.
- 1-year change in serum C-reactive protein (CRP) level and 6-year survival.
- 3-day food record may underestimate actual dietary fat intake at an individual level.
- Higher dietary omega-6 to omega-3 ratio appears to be associated with both worsening inflammation over time and a trend toward higher death risk in hemodialysis patients. Additional studies including interventional trials are needed to examine the association of dietary fatty acids with clinical outcomes in these patients

Noori N, et al. Dietary omega-3 fatty acid, ratio of omega-6 to omega-3 intake, inflammation, and survival in long-term hemodialysis patients. *Am J Kidney Dis*. 2011;58(2):248-256

37

Resistance training vs cachexia and sarcopenia

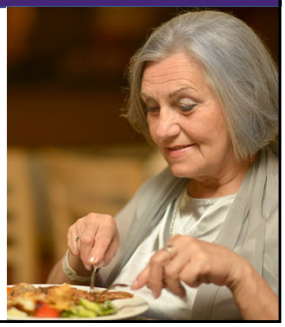
- Resistive exercise (RE) with or without nutritional interventions is a valuable and underutilized tool for improving muscle mass, muscle strength, and physical function in CKD
- Adding high-protein ONS or vitamin D to RE have possible added benefits

Noor, Hanaa et al. "Resistance exercise and nutritional interventions for augmenting sarcopenia outcomes in chronic kidney disease: a narrative review." *Journal of cachexia, sarcopenia and muscle* vol. 12,6 (2021): 1921-1940. doi:10.1002/jcsm.12791

38

Diet counseling

- First Era: Potassium
  - Dialysis Efficiency
  - Less frequent deaths
- Second Era: Phosphate
  - Calcification
- Third Era: Malnutrition
  - Eating more may not be enough

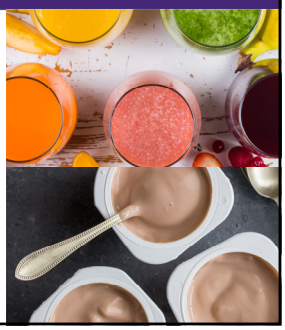


Piccoli, Giorgina Barbara et al. "The Diet and Haemodialysis Dyad: Three Eras, Four Open Questions and Four Paradoxes. A Narrative Review, Towards a Personalized, Patient-Centered Approach." *Nutrients* vol. 9,4 372. 10 Apr. 2017, doi:10.3390/nu9040372

39

PO supplements

- Initial intervention
- Readily available and convenient
- Adherence to oral supplements is variable and low



40

PO supplements: Cochrane review

- 22 studies and 1278 participants, 79%HD, 21%PD
- The rise in serum albumin was more evident in participants who were on HD compared to PD, and those who were malnourished
- Cost outcomes were associated with clinically relevant benefits such as improved quality of life, reduced infections, reduced minor post-operative complications, reduced falls, and functional limitations

Han, Jia Yee et al. "Oral protein-based supplements versus placebo or no treatment for people with chronic kidney disease requiring dialysis." *The Cochrane database of systematic reviews* vol. 5,5 CD012618. 11 May. 2020, doi:10.1002/14651858.CD012618.pub2
Rao, M et al. "A systematic review of the cost and cost effectiveness of using standard oral nutritional supplements in community and care home settings." *Clinical nutrition (Edinburgh, Scotland)* vol. 35,1 (2016): 125-137. doi:10.1016/j.clnu.2015.07.013

41

K/DOQI 2020 implementation considerations: Oral nutrition supplements

- ONS should be prescribed as needed to maximize calorie and/or protein intake to meet daily energy needs.
  - Tailor prescription to patient needs: on MHD days or up to 1-x/day
- Patients should be advised to take ONS 1 hour after meals rather than as a meal replacement to maximize benefit.
- ONS prescription should take into account patient preference and available resources to allow them to purchase products that fit their needs.
- Energy-dense or low-electrolyte renal-specific ON may be necessary to increase protein and energy intake and avoid fluid overload and electrolyte derangements.
- Monitored provision of high-protein meals or ONS during MHD may be a useful strategy to increase total protein and energy intake.

Ikizler, T Alp et al. "KDOQI Clinical Practice Guideline for Nutrition in CKD: 2020 Update." *American journal of kidney diseases : the official journal of the National Kidney Foundation* vol. 76,3 Suppl 1 (2020): S1-S107.

42

Conclusion

- Inflammation is multifactorial and virtually inevitable in CKD and Dialysis
- First, treat underlying inflammation and comorbidities
- Personalize patient's nutrition:
  - Adjust type of cooking (AGE)
    - Recommend boiling, poaching, steaming or stewing
  - Consider concentrated liquid protein medical foods
  - Suggest recipes with ONS/medical foods to increase variety and fight flavor fatigue
  - Consider micronutrients
- Involve family

43

Bibliography

Ikizler, T Alp. "Nutrition, inflammation and chronic kidney disease." *Current opinion in nephrology and hypertension* vol. 17,2 (2008): 162-7.

Yamada, Shunsuke et al. "Emerging cross-talks between chronic kidney disease-mineral and bone disorder (CKD-MBD) and malnutrition-inflammation complex syndrome (MICS) in patients receiving dialysis." Clinical and experimental nephrology vol. 26,7 (2022): 613-629.

Liu, Siyi et al. "Serum C-reactive protein to albumin ratio and mortality associated with peritoneal dialysis." Renal failure vol. 42,1 (2020): 600-606.

Valga, Francisco et al. "Inflammation and hemodialysis adequacy: Are C-reactive protein levels influenced by dialysis dose?." "Inflamación y adecuación de la hemodiálisis: ¿están los niveles de proteína C reactiva influidos por la dosis de diálisis recibida?." Nefrologia, S0211-6995(21)00112-0. 5 Jul. 2021.

Cueto-Manzano, Alfonso M et al. "Systemic inflammation May limit the effect of protein supplement on nutritional status in peritoneal dialysis." *Clinical nutrition ESPEN* vol. 49 (2022): 307-313.

Romão JE Jr, et al. Positive acute-phase inflammatory markers in different stages of chronic kidney disease. *Am J Nephrol.* 2006;26(1):59-66.

Sergi D, Boulestin H, Campbell FM, Williams LM. The Role of Dietary Advanced Glycation End Products in Metabolic Dysfunction. Mol Nutr Food Res. 2021;65(1):e1900934.

Vlassara H, et al. Protection against loss of innate defenses in adulthood by low advanced glycation end products (AGE) intake: role of the anti-inflammatory AGE receptor-1. *J Clin Endocrinol Metab.* 2009;94(11):4483-4491

Uribarri, Jaime et al. "Advanced glycation end products in foods and a practical guide to their reduction in the diet." *Journal of the American Dietetic Association* vol. 110,6 (2010): 911-16.

Foley RN, Wang C, Ishani A, Collins AJ. NHANES III: influence of race on GFR thresholds and detection of metabolic abnormalities. *J Am Soc Nephrol.* 2007;18(9):2575-2582. doi:10.1681/ASN.2006121411

Brooks GC, Blaha MJ, Blumenthal RS. Relation of C-reactive protein to abdominal adiposity. Am J Cardiol. 2010;106(1):56–61

Borah MF, et al. Nitrogen balance during intermittent dialysis therapy of uremia. *Kidney Int.* 1978;14(5):491-500

Cao H, Ye H, Sun Z. Et al., Circulatory mitochondrial DNA is a pro-inflammatory agent in maintenance hemodialysis patients. PloS One. 2014;9(12):e113179

Studart MMMQ, Furioso ACT, Veiga JPR, Rodrigues ME, Gomes LO, Moraes CF. Impact of different automated peritoneal dialysis modalities on the inflammatory profile of elderly patients with chronic kidney disease [published online ahead of print, 2022 Jun 13]. J Bras Nefrol. 2022;S0101-28002022005003401.

Elia, M et al. "A systematic review of the cost and cost effectiveness of using standard oral nutritional supplements in community and care home settings." *Clinical nutrition (Edinburgh, Scotland)* vol. 35,1 (2016): 125-137. doi:10.1016/j.clnu.2015.07.012

Ikizler, T Alp et al. "KDOQI Clinical Practice Guideline for Nutrition in CKD: 2020 Update." *American journal of kidney diseases : the official journal of the National Kidney Foundation* vol. 76,3 Suppl 1 (2020): S1-S107.

44

Bibliography

Lai KN, Leung JC. Inflammation in peritoneal dialysis. *Nephron Clin Pract.* 2010;116(1):c11-c18

Ikizler TA, et al. Prevention and treatment of protein energy wasting in chronic kidney disease patients: a consensus statement by the International Society of Renal Nutrition and Metabolism. *Kidney Int.* 2013;84(6):1096-1107

Icardi A, Paoletti E, De Nicola L, Mazzaferro S, Russo R, Cozzolino M. Renal anaemia and EPO hyporesponsiveness associated with vitamin D deficiency: the potential role of inflammation. Nephrol Dial Transplant. 2013 Jul;28(7):1672–9.

González-Ortiz, Ailema et al. "Relationship between protein-energy wasting in adults with chronic hemodialysis and the response to treatment with erythropoietin." *BMC nephrology* vol. 20,1 316. 14 Aug. 2019

Locatelli F, et al. Nutritional-inflammation status and resistance to erythropoietin therapy in haemodialysis patients. *Nephrol Dial Transplant.* 2006;21(4):991-998

Agarwal R, Davis JL, Smith L. Serum albumin is strongly associated with erythropoietin sensitivity in hemodialysis patients. *Clin J Am Soc Nephrol.* 2008;3(1):98-104

Waldron, Jenna Louise et al. "Vitamin D: a negative acute phase reactant." *Journal of clinical pathology* vol. 66,7 (2013): 620-2. doi:10.1136/jclinpath-2012-201301

Zitt, Emanuel et al. "Efficacy and safety of body weight-adapted oral cholecalciferol substitution in dialysis patients with vitamin D deficiency." BMC nephrology vol. 16 128. 4 Aug. 2015, doi:10.1186/s12882-015-0116-3

Hu, Chun et al. "Effects of Omega-3 Fatty Acids on Markers of Inflammation in Patients With Chronic Kidney Disease: A Controversial Issue." Therapeutic apheresis and dialysis : official peer-reviewed journal of the International Society for Apheresis, the Japanese Society for Apheresis, the Japanese Society for Dialysis Therapy vol. 22,2 (2018): 124-132. doi:10.1111/1744-9987.12611

Noori N, et al. Dietary omega-3 fatty acid, ratio of omega-6 to omega-3 intake, inflammation, and survival in long-term hemodialysis patients. *Am J Kidney Dis.* 2011;58(2):248-256

Noor, Hanaa et al. "Resistance exercise and nutritional interventions for augmenting sarcopenia outcomes in chronic kidney disease: a narrative review." *Journal of cachexia, sarcopenia and muscle* vol. 12,6 (2021): 1621-1640

Piccoli, Giorgina Barbara et al. "The Diet and Haemodialysis Dyad: Three Eras, Four Open Questions and Four Paradoxes. A Narrative Review, Towards a Personalized, Patient-Centered Approach." Nutrients vol. 9,4 372. 10 Apr. 2017

Mah, Jia Yee et al. "Oral protein-based supplements versus placebo or no treatment for people with chronic kidney disease requiring dialysis." *The Cochrane database of systematic reviews* vol. 5,5 CD012616. 11 May. 2020

45