

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

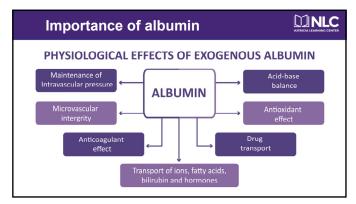
No conflict of interest for this presentation

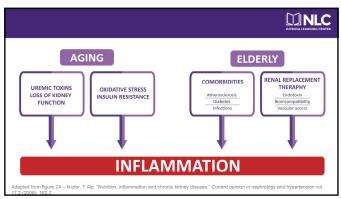
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Objectives



- □ 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





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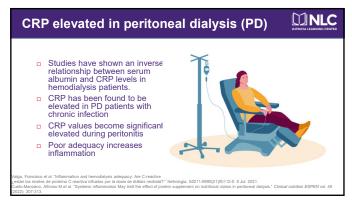
Malnutrition-Inflammation Complex Syndrome (MICS) Protein-energy malnutrition and inflammation that occur concurrently and coexist in individuals with CKD Malnutrition-inflammation-atherosclerosis syndrome (MIA) is also used to describe the combination of malnutrition, inflammation and atherosclerosis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

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.

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

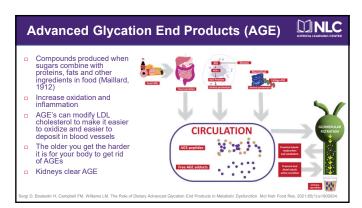
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CRP in peritoneal dialysis	UTRICIA LEARNING CENTER
 34 malnourished patients(SGA) 6 months nutrition counselling + protein supplements (Ealburnin) Two groups based on C-reactive protein (hsCRP) 	igg
 Inflammation (>3 mg/L) 70% improved, 25% no change 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. Cl 313.	lin Nutr ESPEN. 2022;49:307-

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

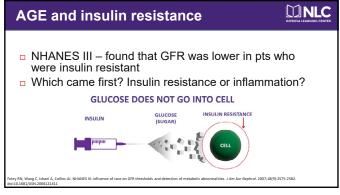
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Role of diet and AGE levels	DI NLC WUTRICIA LEARNING CENTER
Restriction of AGE in diet to prevent DM, CKD and atherois extrapolated.	sclerosis
 Cross sectional with 2-year F/U of healthy adults and C patients 325 healthy adults and 66 CKD-3 patients Diet modifications Results: Reducing dietary AGE intake significantly decreases oxidal in both healthy participants and CKD-3 	
Viassara H, et al. Protection against loss of innate defenses in adulthood by low advanced glycation end products (AGE) into the anti-inflammatory AGE receptor-1. J Clin Endocrinol Metab. 2009;94(11):4483-4491	ke: role of



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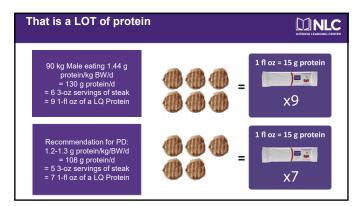




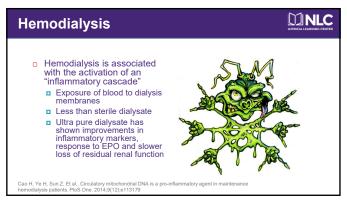
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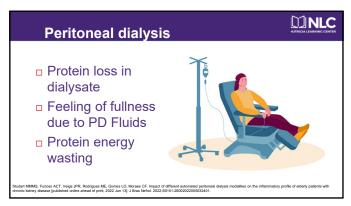


 Borah et al – study on nitrogen balance(1978) High (1.44 g/kg/d) and low protein diets (0.5 g/kg/d) Low, always negative nitrogen balance High in negative nitrogen balance on dialysis days only The process of dialysis increases CRP and IL-6 Inflammatory acute phase reactants markers 	The advent of discussions about nitrogen balance	UTRICIA LEARNING CENTER
□ Inflammatory acute phase reactants markers	 High (1.44 g/kg/d) and low protein diets (0.5 Low, always negative nitrogen balance High in negative nitrogen balance on dialysis only 	g/kg/d) s days
Borah MF, et al. Nitrogen balance during intermittent dialysis therapy of uremia. Kidney Int. 1978;14(5):491-500.		8

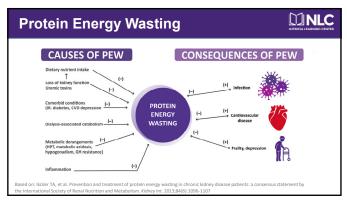


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Does the dialysis solution play a role in inflammation? Glucose Degradation Products (GDP) in dialysate lead to inflammation and then fibrosis GDP's in the dialysis solution and the reactive carbonyl compounds in uremia lead to AGE Authors suggest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



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

kizler 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

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Anorexia

NLC

- A metabolic effect of inflammation
- Animal studies have shown that cytokines have a direct effect on the satiety center
- \blacksquare 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.

ard 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 al Transplant 2013. Int 28(7):1672-8

RU124 Lloyd will buy image once deck is approved. REICHERT Ulrike, 7/22/2022

RU125 [@PRUDENTE Lloyd] slide deck is final, can you please buy the images? REICHERT Ulrike, 8/3/2022

dose and appetite

Anemia and nutritional status	NUTRICIA LEARNING CENTER
Improving nutritional state in dialysis patie may also improve anemia and lead to low required EPO dose.	
 2019 González-Ortiz et al, 61 HD PEW is incremental predictor of poor responsiven EPO in HD patients 	
Gonzálic Ortz, Allema et al. "Ballationiship between protein-energy wording in adults with chronic hemodalysis and the regionar to treatment with erythroposetin." BMC ne 2016, dols 30 1186/11882 059-16170	rephrology vol. 20,1 316: 14 Aug.
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Albumin management and ESA use	UTRICIA LEARNING CENTER
☐ There is an inverse relationship between	ESA

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How do RD's effect EPO usage? Better nutrition status = better EPO responsiveness Our responsibility for addressing inflammation

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

 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

realized by tripling the dose of ESAs



What do CKD patients die of? Cardiovascular mortality Uremic dyslipidemia Infection Malnutrition and failure to thrive

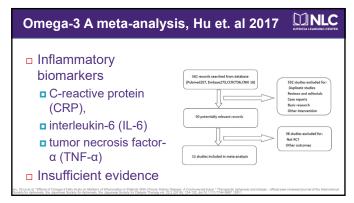
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What can be done to reduce inflammation and increase qol? Uitamin D Omega's Exercise Diet counseling Enteral nutrition

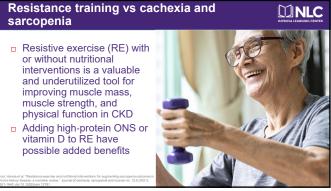
Vitamin D	C NTER
 Starts decreasing in Stage III In Stage VI the median is 15-20 ng/ml Vitamin D is an acute phase reactant – levels decrease with inflammation Which came first? Inflammation = low Vit D 	
■ Low vit D = Inflammation	
Waldron, Jenna Louise et al. "Vitamin D: a negative acute phase reactant." Journal of clinical porthology vol. 66,7 (2013): 620-2. doi:10.1136/jclinpath-2012-201301	

Oral cholecalciferol in dialysis patients with vitamin D deficiency □ 56 patients' baseline 25OHD₃ level <20 ng/mL □ 100 IU of cholecalciferol per kg body weight once weekly orally for 26 weeks □ 25OHD₃ 9.9 → 26.1 ng/mL □ Cinacalcet therapy was positively associated □ iPTH level significantly decreased from median 362 pg/mL to 297 pg/mL

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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 onega-3 compared with omega-46 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 hemodiallysis 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 Klóney Dis. 2011;58(2):248-256			



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

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

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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

Mab, Jia Yee et al. "Onli protein-bassed supplementa venus placebo or no Inselment for people with chronic kitney disease requiring dislysis." The Cochrane debbase of systematic reviews vol. 5,5 C0012895. 11 May, 2005, doi: 10.1002/14651585.C0012895.pdb
Elia, M et al. "A systematic review of the cost and cost effectiveness of using shedred cost institutional appliers ents in community and one home seelings." Chinari Institution (Schichurgh, Scotland) vol. 32, 1, 2016); 125-137. doi: 10.1016/j.chu.2015.07.012

Elia, M et al. "A systematic review of the cost and cost effectiveness of using shedred cost institutional appliers ents in community and one home seelings." Chinari Institution (Schichurgh, Scotland) vol. 32, 1, 2016); 125-137. doi: 10.1016/j.chu.2015.07.012

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K/DOQI 2020 implementation considerations: Oral nutrition supplements



- ONS should be prescribed as needed to maximize calorie and/or protein intoke to most drilly energy people.
- 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.

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

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

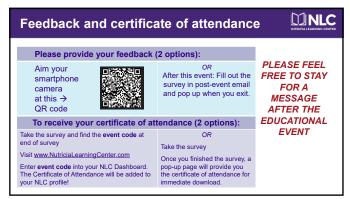
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This ends the educational part of our webinar.

The following short message is about Nutricia's product offerings related to the discussed topic. Please feel free to join us.

