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DOES THE ADVANCED GLYCATION END PRODUCTS FOOD INTAKE INFLUENCE MORTALITY IN DIALYSIS PATIENTS?

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Abstract

Advanced glycation end products (AGEs) are considered as uremic toxins and contribute to cardiovascular complications in HD patients. Consumption of specific foods is associated with increased AGEs. In this study we investigated the AGE food consumption as a potential risk of mortality in dialysis patients.

A study group of 150 dialysis patients were asked to fill in a 7-day diet questionnaire where from the data on protein, calorie and AGEs daily food intakes were extrapolated. Patients were followed for 36 months. Kaplan-Meier survival curves were applied to estimate difference in survival in patients with low (below median intake), or high (above median intake) of AGEs. The median CRP level was obtained for survival correction by inflammation.

The mean age of study participants was 55 years and 62% of them were men. The average amount of daily intake of AGEs was 9.4 ± 4.0 MU/24 hours. The average daily protein and calories intake were within current recommendations. The median level of daily AGEs intake was 8.9 MU/day. When patients were stratified by AGEs rich or poor diet and inflammatory state, no difference for survival was found in all groups. Patients with high inflammation did not differ in survival in relation to rich or poor AGEs diet (p=0.614). In patients with low CRP better survival had patients consuming more AGEs, but the difference was not statistically significant (p= 0.167).

Inflammation strongly impacts survival of dialysis patients. Rich AGEs food diet was not found to be at risk of mortality. Traditional diet explains better outcomes in dialysis patients.

Keywords: mortality, survival, dialysis, advanced glycation end products, inflammation.

Introduction

Advanced glycation end products (AGEs) are considered as uremic toxins and contribute to cardiovascular complications of HD patients [1, 2]. Consumption of specific foods is associated with increased AGEs. Food AGEs content depends on the quality, quantity of food and also the way of preparation [3]. Efforts are being done towards modelling a diet low in these products, as a way of improving life span [4]. The link between nutrition, body mass index and AGEs from food was found to be in a linear correlation [5]. Dialysis patients suffer from malnutrition. Protein energy wasting is one of the independent risk factors associated with high mortality rate [6]. In this study we investigated the AGE food consumption as a potential risk of mortality in dialysis patients.

Material and methods

A study group of 150 dialysis patients were asked to fill in a 7-day diet questionnaire. Patients were advised for food and portions recording. Daily AGEs intake was estimated by Goldbergs tables [3], which were adapted to traditional local meals. The protein and calorie intake per day were estimated from tables by the United States Department of Agriculture Nutrition's Database [7]. Dialysis, nutritional and laboratory variables were used from patients' regular monthly sheets and medical history. Patients were followed for 36 months until death, transplantation or change of dialysis modality. Statistical analysis: Continuous variables are shown as mean values and categorical as percentages. Kaplan-Meier survival curves were applied to estimate difference in survival in patients with low (below median intake), or high (above median intake) AGEs. The median CRP level was obtained for survival correction by inflammation. Inflammation strongly impacts survival of dialysis patients. Rich AGEs food diet was not found to be at risk of mortality. Traditional diet explains better outcomes in dialysis patients.

Results

The mean age of study participants was 55 years and 62% of them were men (Tab.1). On average, patients were dialyzed for more than 8 years and the vast majority achieved good dialysis

adequacy. Renal anemia was treated with erythropoietin and the mean hemoglobin level of the population was well – 116 g/L. The nutritional indices as albumin and BMI were in target ranges. The values of C-reactive protein (CRP) as marker of inflammation showed marked variations between subjects.

Table 1. Demographic, dialysis and nutritional indices of study population

N=150	Mean	St. Dev.
Male	94 (62%)	
Age (years)	55.69	13.5
Vintage (years)	8.89	5.78
KT/V	1,38	0.2
Hb (g/l)	116.17	8.6
Ab (g/L)	38.8	2.7
CRP (mg/L)	7.21	8.73
BMI (Kg/m²)	23.25	4.6

The average amount of daily intake of AGEs was 9.4 ± 4.0 MU/24 hours. The average daily protein intake per body weight was 1.27 ± 0.68 g/24hours/Kg and calorie intake 30.27 ± 9.4 kcal/24h/kg. The median level of daily AGEs intake was 8.9 MU/day. There were 76 patients consuming AGEs rich diet and 74 patients consuming AGEs low diet. In the follow up period 49 (33%) of patients died. In the AGEs rich diet group 25 (26%) died and similar number of deaths occurred in the AGEs low diet group (24 (32%)), respectively. When patient's survival was analyzed in relation to low or high daily AGEs food intake by median level, no difference was found in both groups (32.9 months *vs*. 33.7 months, p= 0.627), (Fig. 1).

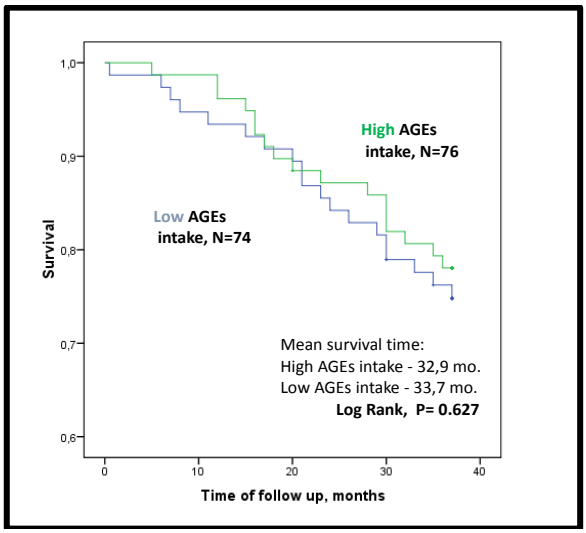

Figure 1. Kaplan-Meier estimates of survival with regard to all-cause mortality in relation to low (below median intake), or high (above median intake) of Advanced Glycation End Products (AGEs).

Patients survival was seriously affected by inflammation (Fig.2). When patients were dived by CRP median level (4.6 mg/L), 76 patients showed high and 74 patients' low inflammatory status. The mortality was lower in the group of patients with low than high CRP (21 (28%) vs (28 (36%)) and survival was significantly better in patients with lower inflammation (32.0 months vs. 34.4 months, p= 0.038).

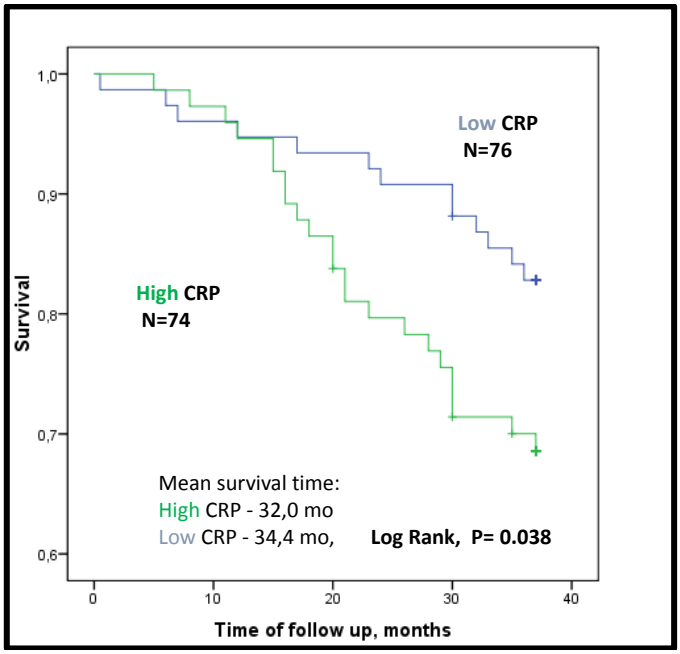

Figure 2. Kaplan-Meier estimates of survival with regard to all-cause mortality in relation to low (below median levels), or high (above median levels) of CRP.

When patients were stratified by AGEs rich or poor diet and inflammatory state, no difference for survival was found in all groups (Fig.3). Patients with high inflammation did not differ in survival in relation to rich or poor AGEs diet (p=0.614). In patients with low CRP better survival had patents consuming more AGEs, but the difference was not statistically significant (p= 0.167).

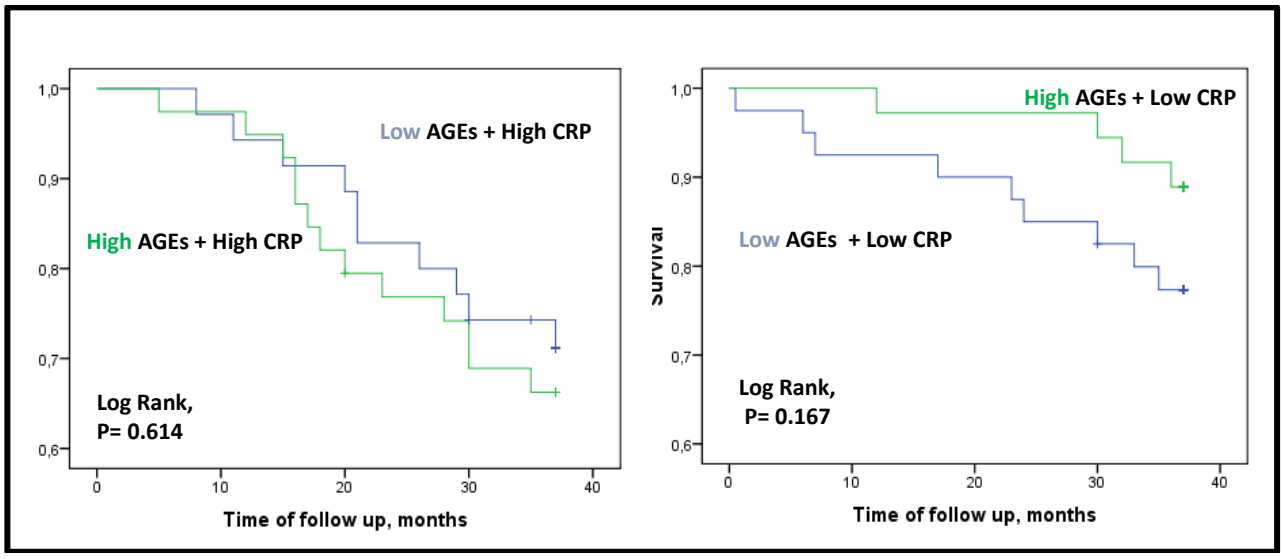

Figure 3. Kaplan-Meier estimates of survival with regard to all-cause mortality in relation to different combinations of low (below median levels), or high (above median levels) of CRP and low (below median intake), or high (above median intake) AGEs.

Discussion

The role of chronic inflammation in related adverse cardiovascular outcomes and high mortality rate of dialysis patients have been demonstrated in many studies, and several pathogenetic mechanisms have been introduced in this regard. Mortality is influenced by interaction of nutrition, inflammation and comorbidities [8,9,10]. As a marker of inflammatory status, in many studies CRP

showed wide range of standard deviation [11]. Our study confirmed those results and also the connection of CRP with mortality. The group of patients with less inflammation lived longer in our study. The present K/DOQI clinical practice guideline for hemodialysis suggested stabilized serum albumin equal to or greater than 4.0 g/dL [12]. Our patients presented with well-preserved albumin levels. Low hemoglobin level and erythropoiesis-stimulating agents could lead to cardiovascular events, fatigue, and even mortality, while low serum albumin level in dialysis patients is also known to be associated with malnutrition, inflammation, and all-cause and cardiovascular mortality [13]. Our results showed appropriate achievement of target hemoglobin level in vast majority of patients. Arsov *et al*. found that calories, protein and AGEs intake hardly influence the AGE products body accumulation. BMI of dialysis patients of around 24 kg/m^2 resulted in a lower accumulation [5]. Also, this study showed that calories, AGE and protein intake correlated with each other. Another study showed that patients consuming less than 16 MU/24 hours survived longer [4]. The daily AGE intake of our patients was lower than 12 MU/24 hours. Our survival analysis according to rich or poor AGEs diet showed no difference in life span. When patients were divided according to presence of inflammation in combination with AGEs intake, best survival was seen in patients with rich AGE diet and lower CRP. Since most of the patients had good nutritional indices as BMI, albumin and hemoglobin, and also good calorie and protein intakes, the bigger AGEs intake we understood as better nutritional status. Inflammatory status remained the most influencing factor on mortality.

Conclusion

Inflammation strongly impacts survival of dialysis patients. Rich AGEs food diet was not found to be at risk of mortality. Traditional diet explains better outcomes in dialysis patients.

Refferences

1. Vanholder R, De Smet R, Glorieux G, Argiles A, Baurmeister U, Brunet P, Clark W, Cohen G, De Deyn PP, Deppisch R, et al. Review on uremic toxins: classification, concentration, and interindividual variability. Kidney Int. 2003;63(5):1934–43.
2. Meerwaldt R, Hartog JW, Graaff R, Huisman RJ, Links TP, den Hollander NC, Thorpe SR, Baynes JW, Navis G, Gans RO, et al. Skin autofluorescence, a measure of cumulative metabolic stress and advanced glycation end products, predicts mortality in hemodialysis patients. J Am Soc Nephrol. 2005;16(12):3687–93.
3. Goldberg T, Cai W, Peppa M, Dardaine V, Baliga BS, Uribarri J, Vlassara H. Advanced glycoxidation end products in commonly consumed foods. J Am Diet Assoc. 2004;104 (8):1287–91.
4. 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(6):911–6.
5. Arsov S, Trajceska L, van Oeveren W, Smit AJ, Dzekova P, Stegmayr B, Sikole A, Rakhorst G, Graaff R. The influence of body mass index on the accumulation of advanced glycation end products in hemodialysis patients. Eur J Clin Nutr. 2015; 69(3):410.
6. Bonanni, A., Mannucci, I., Verzola, D. et al. Protein-energy wasting and mortality in chronic kidney disease. Int J Environ Res Public Health. 2011; 8: 1631–54.
7. The United States Department of Agriculture. Nutritive Value of Foods. http://www.ars.usda.gov/SP2UserFiles/Place/12354500/Data/hg72/hg72_2002.pdf. 2002
8. Selim G, Stojceva-Taneva O, Zafirovska K, Sikole A, Gelev S, Dzekova P, et al. Inflammation predicts all-cause and cardiovascular mortality in haemodialysis patients. Prilozi. 2006;27:133–44.
9. Beberashvili I, Sinuani I, Azar A, Yasur H, Shapiro G, Feldman L, et al. IL-6 levels, nutritional status, and mortality in prevalent hemodialysis patients. Clin J Am Soc Nephrol. 2011;6:2253–63.
10. Heidari B. C-reactive protein and other markers of inflammation in hemodialysis patients. Caspian J Intern Med. 2013; 4:611–6.
11. Weng, C. H., Hu, C. C., Yen, T. H. & Huang, W. H. Association between ambient carbon monoxide and secondary hyperparathyroidism in nondiabetic patients

undergoing peritoneal dialysis. Ther Clin Risk Manag; **11**,1401–08, 10.2147/TCRM.S91475 (2015).

12. National Kidney, F. KDOQI Clinical Practice Guideline for Hemodialysis Adequacy: 2015 update. Am J Kidney Dis 66, 884–930.
13. Weng CH, Hu CC, Yen TH, Hsu CW, Huang WH. Nutritional predictors of mortality in long term hemodialysis patients. Sci Rep. 2016; 6: 35639. doi: 10.1038/srep35639.