

VERY LOW PROTEIN DIET SUPPLEMENTED WITH KETOANALOGUES OF ESSENTIAL AMINOACIDS IN CHRONIC KIDNEY DISEASE: A STRATEGY TO SLOW THE LOSS OF RENAL FUNCTION

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BACKGROUND AND OBJECTIVE

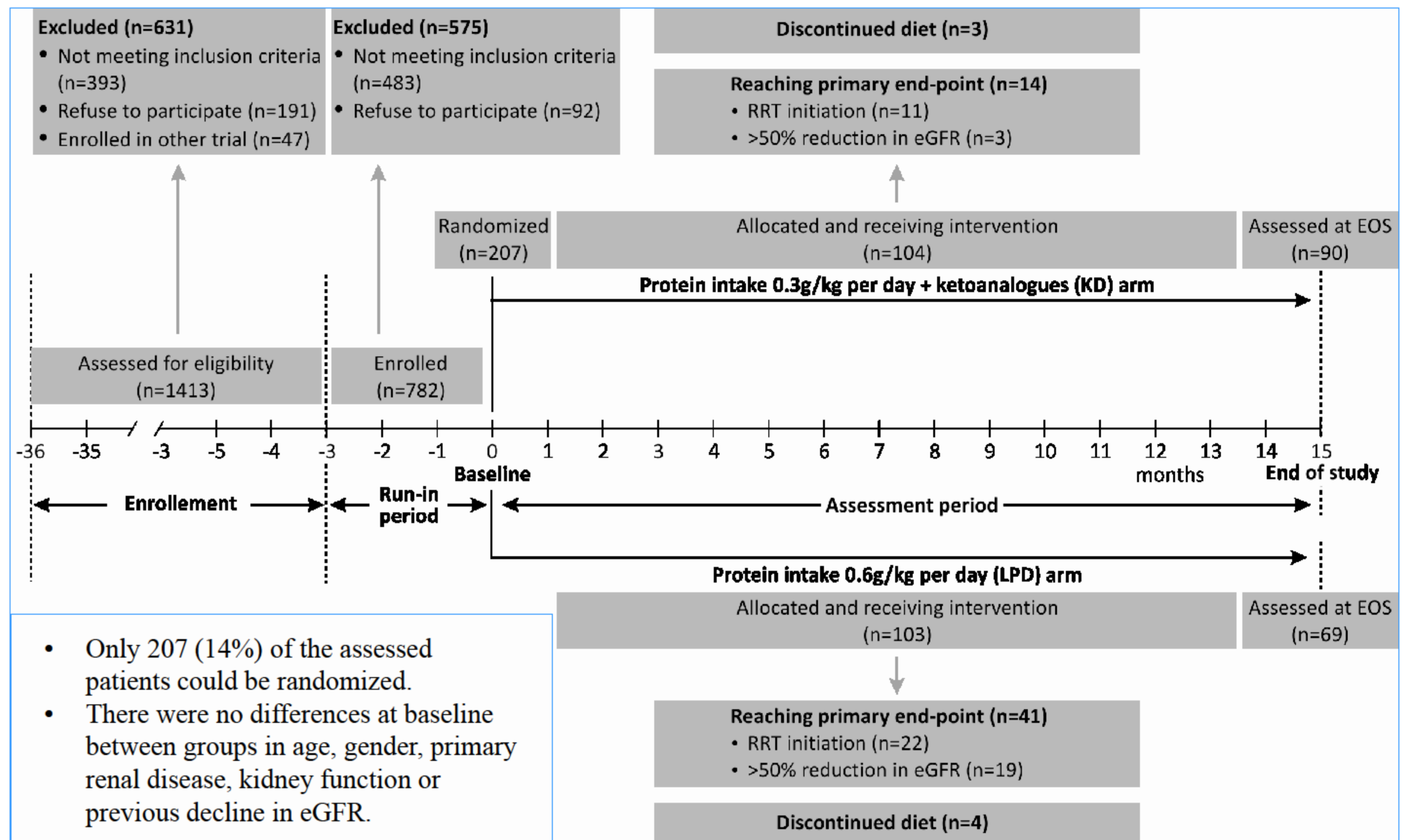
- Protein-restricted diets are used for many decades in advanced Chronic Kidney Disease (CKD) [1-3]. However, their efficacy in improving uremic symptoms and postponing the initiation of renal replacement therapy (RRT), and its safety are still debatable [4-9].
- The aim was to assess effectiveness and safety of a very low protein diet supplemented with ketoanalogues of essential amino-acids (keto-diet, KD) in reducing CKD progression as compared to a conventional low protein diet (LPD).

STUDY DESIGN

- Type:** Prospective, single-center randomized controlled trial
- Parameters:**
 - Efficacy:**
 - Primary composite endpoint: RRT initiation or $\geq 50\%$ reduction in the initial estimated glomerular filtration rate (eGFR)
 - Secondary parameters: RRT initiation, eGFR decline, correction of metabolic disturbances
 - Safety:** nutritional status, dietary compliance, adverse events

SUBJECTS AND METHODS

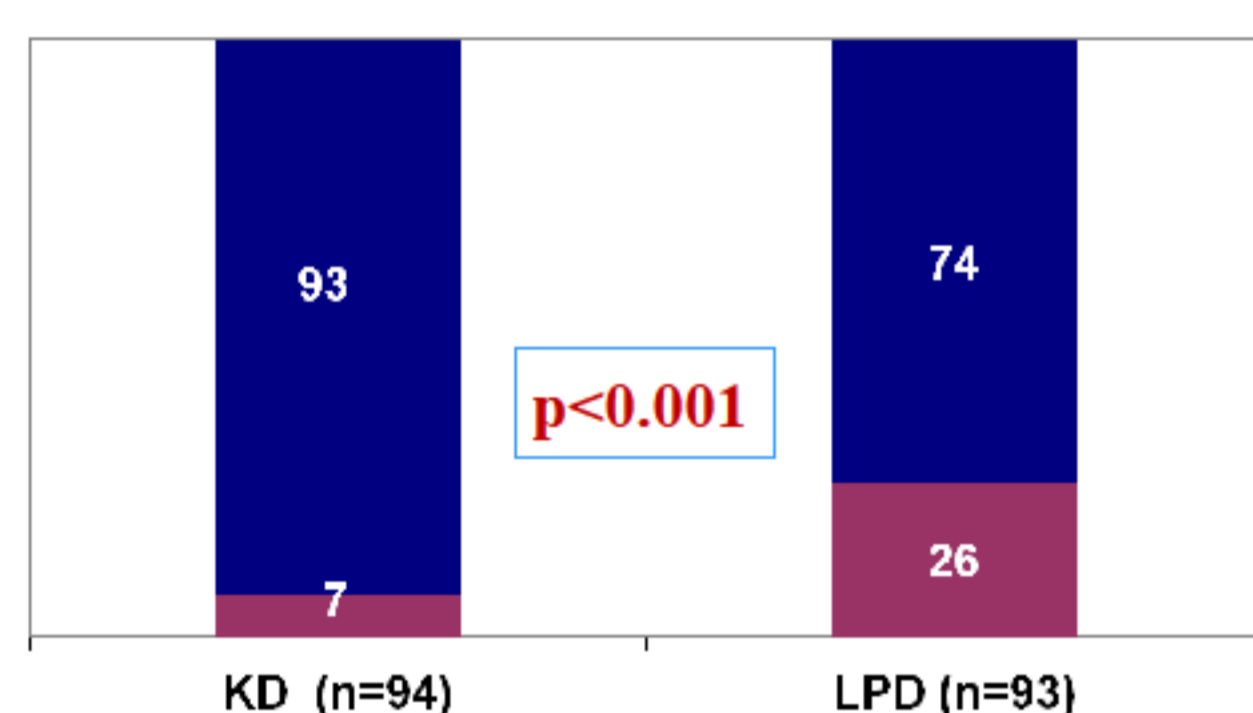
- Non-diabetic adult CKD patients: 63% males, median age 55.0 [44.0-60.0] yrs, eGFR 18.0 [12.4-24.5] mL/min; 57% primary glomerulopathies.
- eGFR < 30 mL/min/1.73m² (MDRD4 formula)
- Proteinuria < 1 g/g urinary creatinine
- Good nutritional status
- Anticipated good compliance to the diet were randomized.



RESULTS

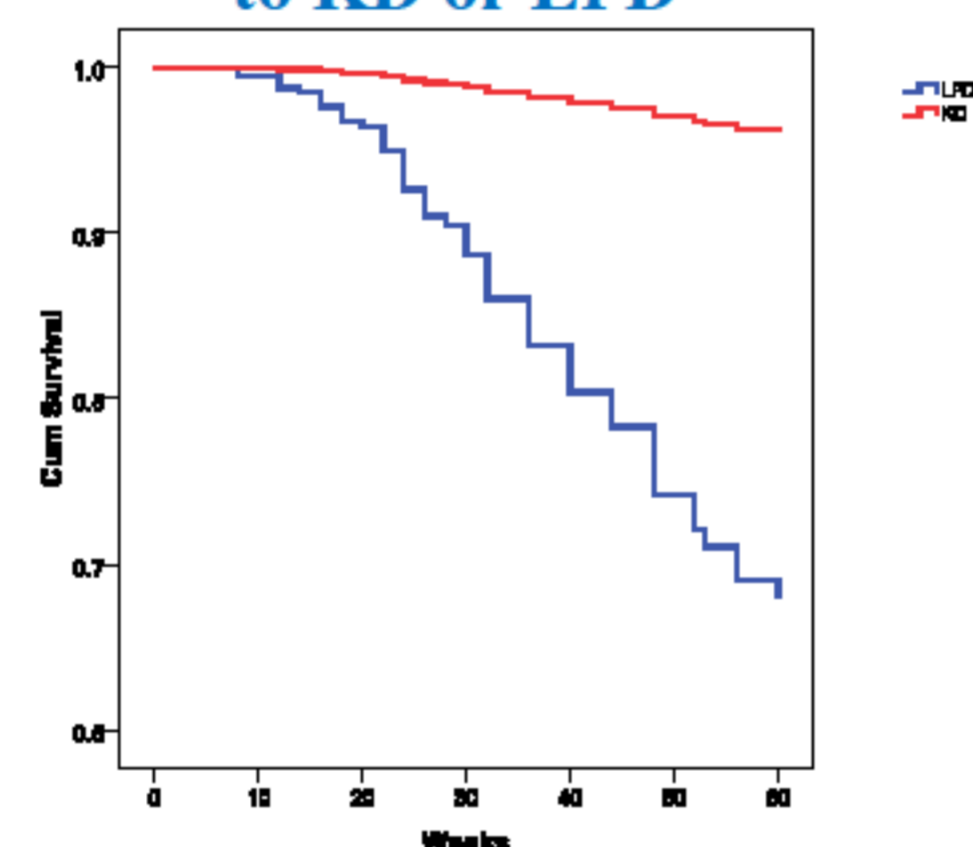
Progression of Chronic Kidney Disease

Patients requiring RRT initiation (%)



- No patients' death was registered.
- Significantly lower percentages of patients in KD Group required RRT.

Adjusted event-free survival rates of patients assigned to KD or LPD



- The cumulative probability to reach the end point during one year was also lower in the KD group: 12 vs. 39%.

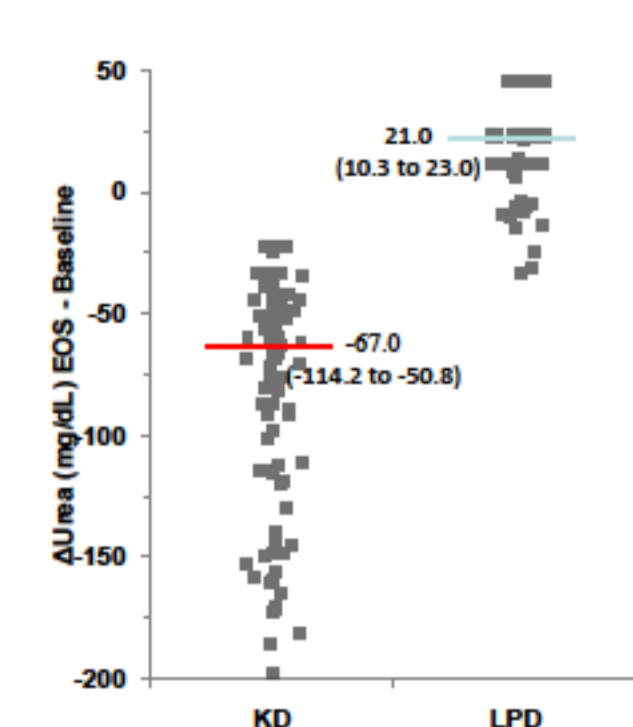
Adjusted number needed to treat (NNT) to avoid the primary end-point and dialysis initiation, according to initial eGFR

eRFG	Intention to treat		Per protocol	
	Primary end-point	Dialysis initiation	Primary end-point	Dialysis initiation
<30mL/min	4.4 (4.2-5.1)	22.4 (21.5-25.1)	4.0 (3.9-4.4)	23.7 (22.8-26.2)
<25mL/min	2.7 (2.5-3.1)	8.0 (7.6-9.2)	2.5 (2.3-2.6)	6.3 (6.1-7.0)
<20mL/min	1.9 (1.7-2.2)	2.2 (2.7-2.6)	1.8 (1.6-2.1)	2.6 (2.4-2.9)
<15mL/min	1.3 (1.4-1.6)	1.6 (1.4-1.2)	1.2 (1.1-1.5)	1.2 (1.1-1.5)

- The NNT to avoid the primary endpoint in ITT and PP analyses were 4.4 and 4.0
- The NNT to avoid dialysis initiation was 22.4, but decreased to 2.7 when only patients with eGFR < 20 mL/min were retained in analysis.

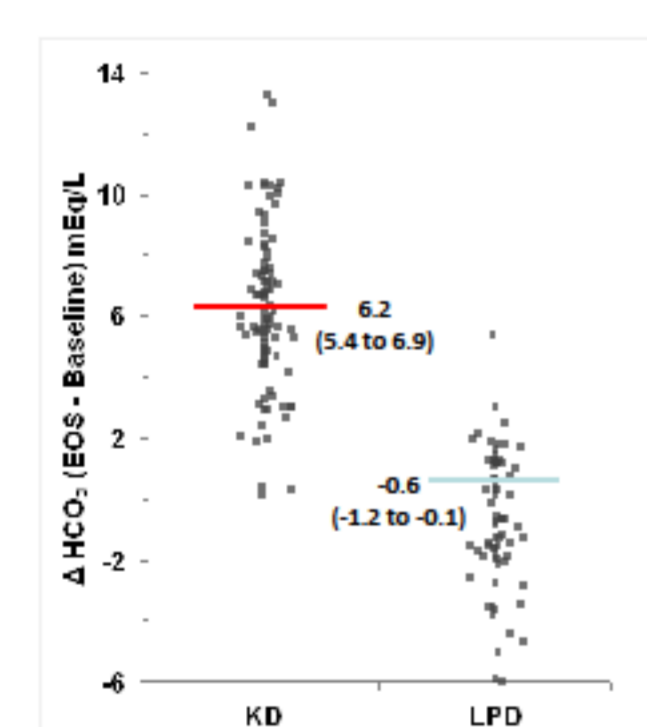
Correction of metabolic disturbances

Nitrogen balance



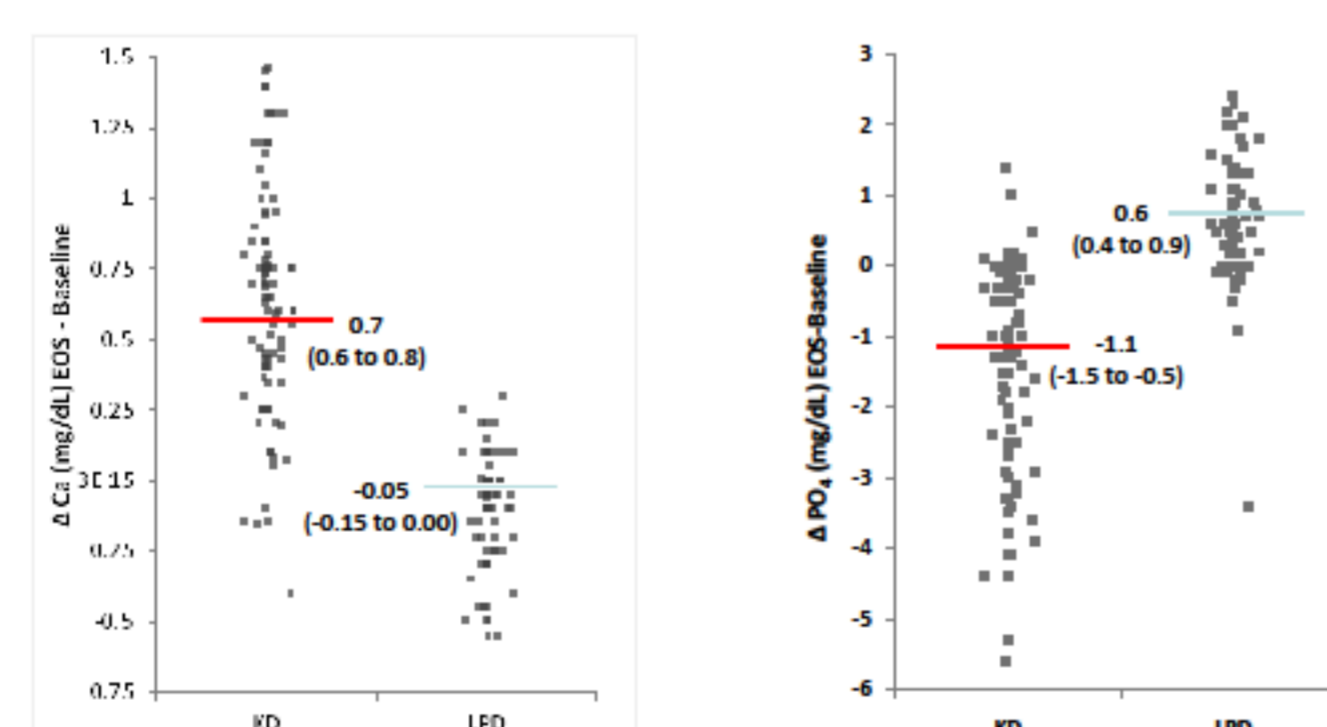
- Serum urea significantly decreased only in the KD group.

Metabolic acidosis



- Serum bicarbonate significantly increased only in patients on KD.

Calcium-phosphorus metabolism abnormalities

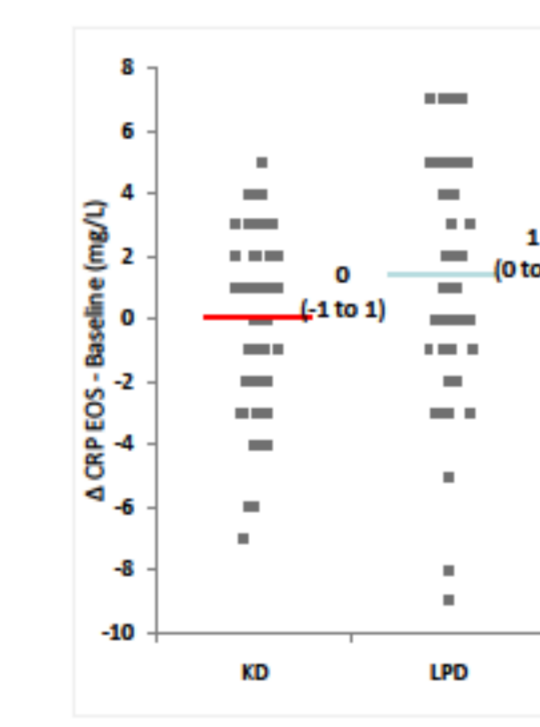


- Serum calcium increased and serum phosphates decreased in KD arm; opposite variations were seen in LPD.

Safety parameters. Compliance to the diet

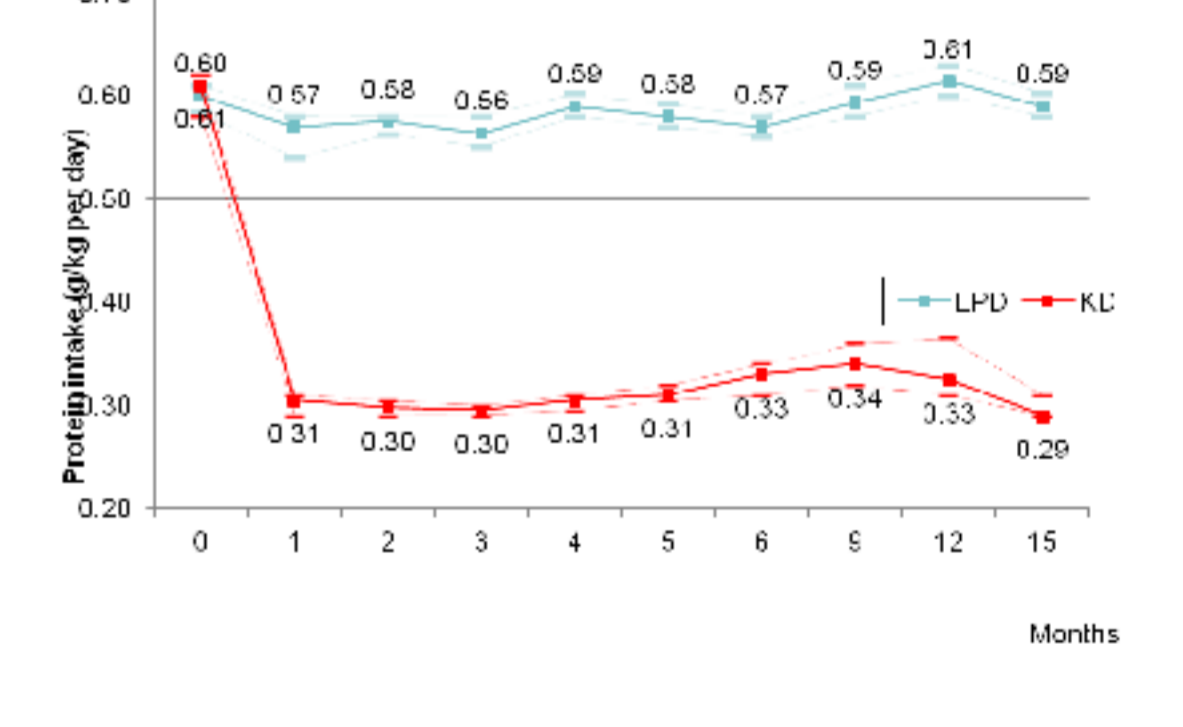
- Only 3% of patients discontinued the diet.
- The compliance to both regimens was good.
- There were no significant changes in any nutritional parameters.
- No adverse reactions were noted.

Inflammation



- CRP was lower at EOS in KD patients; significantly increased in LPD.

Achieved protein intake



- The achieved protein intake was very close to prescription and remained stable throughout the study.

CONCLUSIONS

- Ketoanalogues supplementation allows for a nutritionally safe severe reduction in protein intake which could limit CKD progression by ameliorating its metabolic disturbances, and could defer dialysis initiation in patients with eGFR lower than 20 mL/min. Intensive nutritional counseling and monitoring are necessary to ensure compliance and adherence.

REFERENCES:

- Mitch WE: Dietary protein restriction in chronic renal failure: nutritional efficacy, compliance, and progression of renal insufficiency. *J Am Soc Nephrol* 2:823-831, 1991
- Combe C et al: Compliance and effects of nutritional treatment on progression and metabolic disorders of chronic renal failure. *Nephrol Dial Transplant* 8:412-8, 1993
- Walser M, Hill S: Can Renal Replacement Be Deferred by a Supplemented Very Low Protein Diet? *J Am Soc Nephrol* 10:110-116, 1999
- Fouque D et al: Low protein diets for CKD in non diabetic adults. *Cochrane Database Syst Rev* 3:CD001892, 2009
- Mircescu G et al: Effects of a supplemented hypoproteic diet in CKD. *J Ren Nutr* 17(3):179-188, 2007
- Ikizler A: Dietary protein restriction in CKD: the debate continues. *Am J Kidney Dis* 53(2):189-191, 2009
- Levey AS et al and Modification of Diet in Renal Disease Study Group: Effects of dietary protein restriction on the progression of advanced renal disease in the modification of diet in renal disease study. *Am J Kidney Dis* 27: 652-663, 1996
- Brunori G et al: Efficacy and Safety of a Very-Low-Protein Diet When Postponing Dialysis in the Elderly: A Prospective Randomized Multicenter Controlled Study. *Am J Kidney Dis* 49(5) 569-580, 2007
- Piccoli GB et al: Vegetarian low-protein diets supplemented with ketoanalogues: a niche for the few or an option for many? *Nephrol Dial Transplant* 28:2295-2305, 2013