

EFFECTS OF A REGIMEN BASED ON RESTRICTED CALCIUM INTAKE FROM PHOSPHATE BINDERS, LOW DOSE VITAMIN D SUPPLEMENTATION, AND PARICALCITOL, ON SURVIVAL, HOSPITALIZATION AND RENAL PROGRESSION. A PROSPECTIVE COHORT STUDY FOR CONTROLLING CKD_MBD IN NON-DIALYSIS CKD PATIENTS.

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INTRODUCTION & AIMS

- Although there are an increasing number of studies indicating survival advantages of the use of calcium-free phosphate binders and selective vitamin D (VD) receptor activators in maintenance dialysis patients, little is known if this effect is also present in non-dialysis chronic kidney disease patients (ND-CKD).
- This study compared the effect of a regimen based on restricted Ca intake from phosphate binders and paricalcitol, with unrestricted conventional care (VD and phosphate binders) for the appearance of death, hospitalization and kidney progression in ND-CKD patients.

METHODS

- We conducted a matched-cohort analysis of adults ND-CKD stage 4-5 patients, identified from a database of the Valencian Society of Nephrology.
- We enrolled 249 patients who had received treatment with a paricalcitol-based regimen which limited elemental calcium intake from phosphate binders between Jan 1, 2013, and Dec 31, 2014, and matched them –according to age, gender, comorbidities, CKD-stages, and calcium, phosphorus, iPTH, and 25(OH)D levels– with 498 controls with unrestricted conventional care (vitamin D and phosphate binders) for achieving mineral metabolism.
- All enrolled patients received a treatment protocol for controlling bone metabolism parameters based on the use of:
 - Low doses of calcium acetate and calcium-free phosphate binders for hyperphosphatemia.
 - Moderate doses of oral calcidiol (16000 IU monthly) for vitamin D deficiency.
 - Paricalcitol as the only anti-parathyroid agent.

| CKD-MBD TARGETS | 25 OHD (ng/mL) | 20–40 |
|---------------------------|---------------------------------|-------|
| iPTH (pg/mL) | CKD 4: 70–110 CKD 5: 150–300 | |
| Ca _{alb} (mg/dL) | 8.4–10.2 | |
| P (mg/dL) | 2.3–4.7 | |

- Crude analysis of survival was performed using the Kaplan-Meier method. The univariate and multivariate analyses were conducted by means of Cox proportional hazards model. Death episodes, hospital admissions and kidney progression were prospectively gathered over a 12-month period.

RESULTS

Patients characteristics at baseline

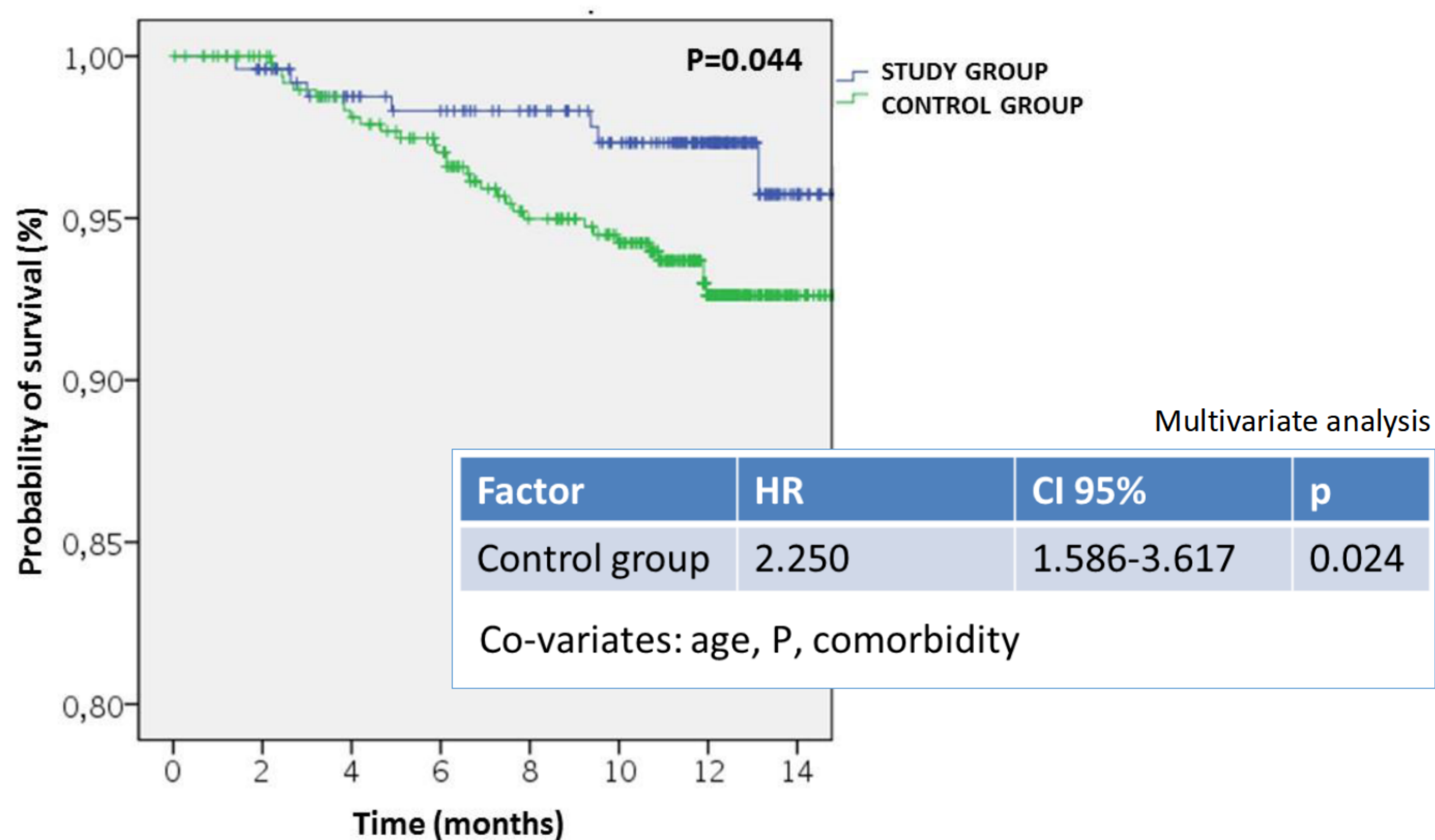
| | Paricalcitol-based regimen with limited Ca intake (n=249) | Control* (n=498) | p |
|--------------------------------------|---|------------------|-------|
| 25D (ng/mL) | 24 (15-32) | 24 (16-31) | 0.744 |
| iPTH (pg/mL) | 150 (99-201) | 134 (86-208) | 0.220 |
| Ca _{alb} (mg/dL) | 9.3 ± 0.6 | 9.4 ± 0.7 | 0.289 |
| P (mg/dL) | 3.9 ± 0.7 | 3.9 ± 0.7 | 0.970 |
| Albúmina (g/dL) | 4.0 ± 0.4 | 4.0 ± 0.5 | 0.336 |
| CKD-EPI (ml/min/1.73m ²) | 19.1 ± 5.6 | 19.0 ± 5.6 | 0.576 |

*Matched by age, gender, comorbidities, CKD-stages, and Ca, P, iPTH, and 25(OH)D levels.

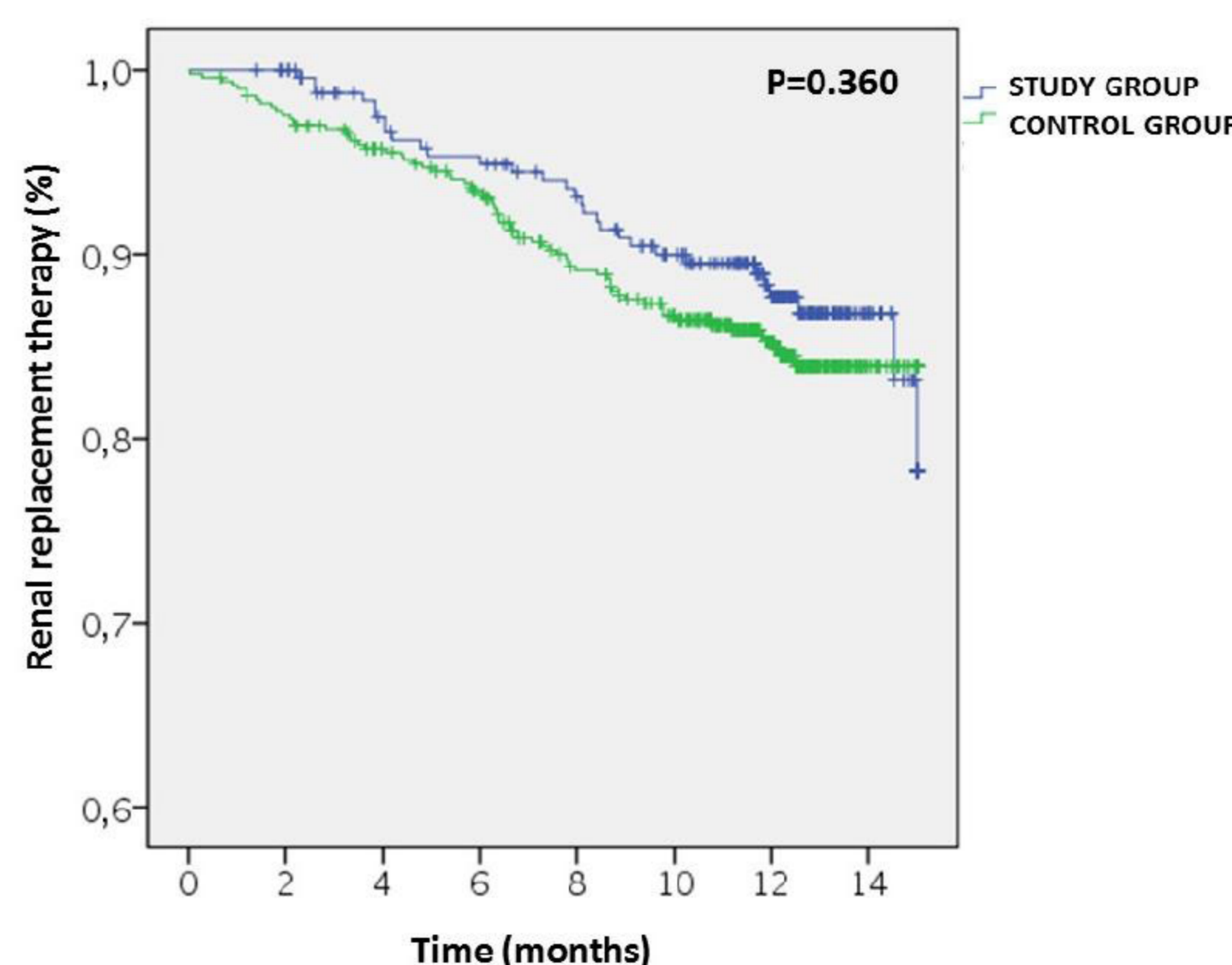
| | Paricalcitol-based regimen with limited Ca intake (n=249) | Control (n=498) | p |
|------------------|---|-----------------|--------|
| Calcitriol | 0% | 32% | n.a. |
| Ca carbonate | 0% | 13% | n.a. |
| Nutritional VitD | 37% | 7% | <0.001 |
| Paricalcitol | 35% | 1% | <0.001 |
| Ca acetate | 10% | 20% | <0.001 |
| Sevelamer | 9% | 6% | 0.086 |
| Lanthanum | 0.9% | 0.2% | 0.237 |
| Aluminium | 1% | 4% | 0.016 |

- At baseline, serum levels of Ca, P, PTH, vitamin D, albumin and eGFR were similar in both groups.
- The use of calcium-free phosphate binders (sevelamer:12% Vs. 5%; p=0.002; lanthanum: 4% Vs. 0%; p=0.001) and paricalcitol (55%Vs.3%;p<0.001) was higher in the study group, whereas the proportion of patients under treatment with calcium carbonate (0% Vs.11%; p<0.001) and calcitriol (0% Vs. 37%; p<0.001) was greater in the control group. Use of calcium acetate was similar in both groups (14% Vs.14%; p=0.398).

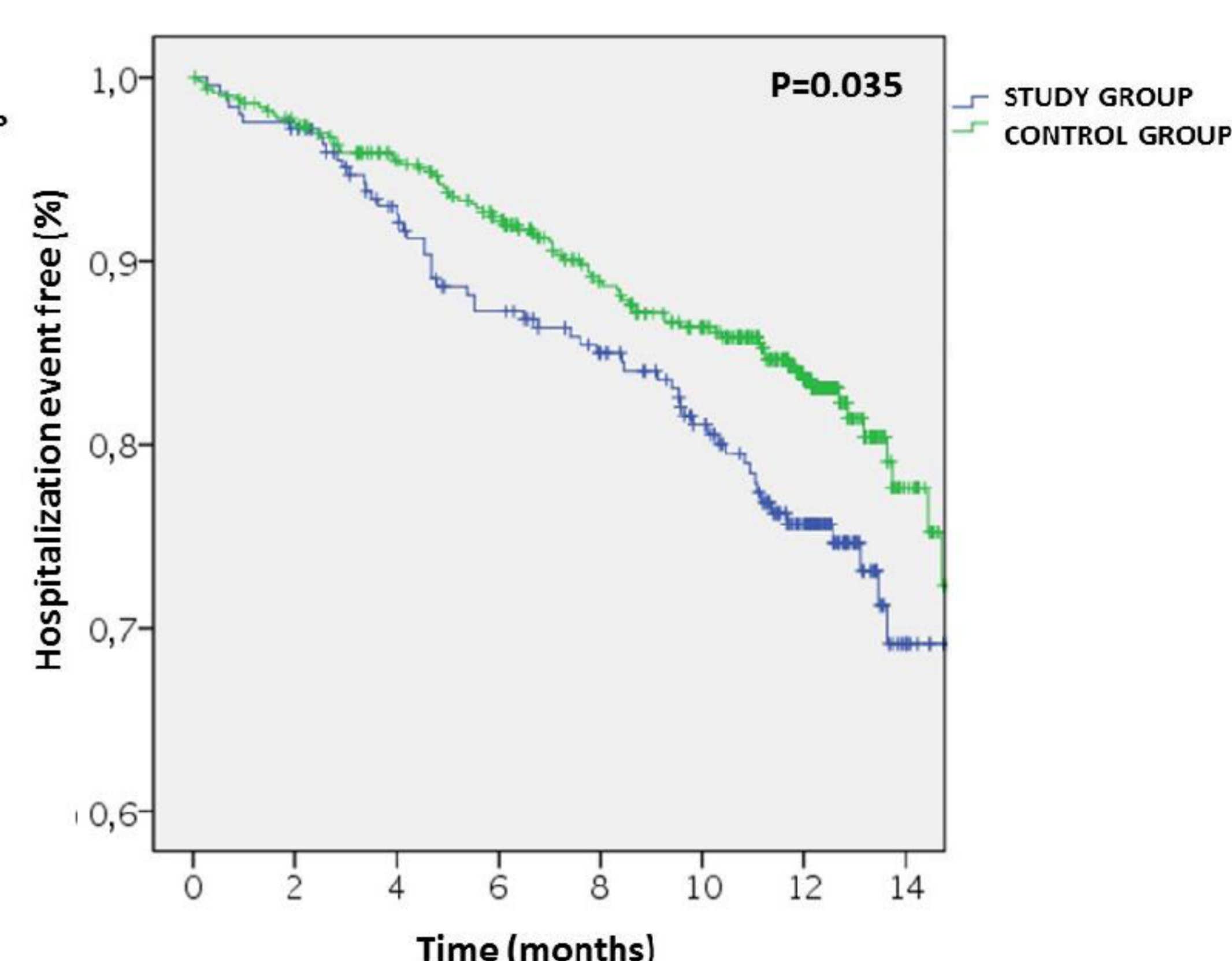
Survival



Renal progression



Hospitalization



- Over 11±3 months of follow up there were 40 deaths (5%), 128 patients (17%) were hospitalized and 102 subjects (14%) started dialysis treatment.
- In the crude analysis, the study group had significantly lower mortality (log rank test, p=0.044) than the control group.
- After multivariate adjustment including age, phosphorous levels, and comorbidities, the study group showed better survival than the control group [HR 0.370 (95%CI: 0.154-0.887); p=0.026].
- No differences were observed in kidney progression and all-cause hospitalization event-free period after adjustment.

CONCLUSIONS

- Compared with unrestricted conventional care, a regimen based on the restricted use of calcium-based binders in combination with calcium-free phosphate binders, low dose nutritional vitamin D supplementation, and the use of paricalcitol as anti-parathyroid agent, was independently associated with better survival in CKD patients.
- Randomized clinical trials are required to confirm our findings.

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