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Introduction and Aims

Previous reports in prevalent hemodialysis (HD) patients indicated that pre-HD serum sodium (SNa⁺) concentrations are stable over time (“SNa⁺ setpoint”; Keen, *Int J Art Organs* 2007). Pre-HD SNa⁺ concentration has been linked to outcomes in HD patients (Waikar, *Am J Med.* 2011) and an increased pre-HD SNa⁺ variability over time has been shown to be related to increased morbidity and mortality. (Raimann, *ERA-EDTA* 2012). We investigated the relation between SNa⁺ variability and hospitalization in incident chronic HD patients.

Methods

This longitudinal cohort study included HD patients in Renal Research Institute clinics in the U.S. who started HD between 1/2001 and 7/2008 who survived at least 18 months. Patients were stratified into three groups of SNa⁺ concentrations (average of SNa⁺ over the first 12 months on HD: <137; 137-141; >141 mEq/L) and three groups of SNa⁺ variability (coefficient of variation (CV) of SNa⁺ over the first 12 months on HD: <10%; 10 to 20%; >20%).

Hospitalizations were recorded during months 13 to month 18. Kaplan Meier analysis was used to estimate time to first hospitalization, stratified by SNa⁺ concentration and CV. Cox regression was used to compute hazard ratios (HR) of hospitalization adjusted for gender, race, age, vascular access, co-morbidities, systolic blood pressure and eKt/V.

Results

We studied 4451 HD patients (age 61±15.21 years, 56% male, 56% diabetic, 43% blacks). Kaplan Meier analysis showed a clear inverse relation between SNa⁺ variability and time to first hospitalization in patients with low SNa⁺ (Fig. 1A, log rank test P<0.001). In patients with mid-range SNa⁺, only the subgroup with high sodium variability had a clearly shorter time to first hospitalization (Fig. 1B, log rank test P=0.02), whereas in patients with high SNa⁺, no significant relationship between sodium variability and hospitalization risk was detected, although there was a trend for shorter time to first hospitalization in patients with medium or high sodium variability (Fig. 1C). Multivariable

Cox regression indicated that patients in the (SNa⁺<137, CV>20%) group had a 40% increased risk of hospitalization compared to the reference group (SNa⁺ 137-141, CV<10%), (P=0.011). The results suggest a trend for higher risk of hospitalization with higher sodium variability, particularly in patients with low SNa⁺ (Table 1).

Conclusion

Our analyses suggest a trend for higher risk of hospitalization in patients with higher SNa⁺ variability. This appears particularly pronounced in patients with low SNa⁺ concentrations, whereas higher SNa⁺ levels appear to blunt this relationship. Correlates of higher SNa⁺ variability should be investigated, and future studies should also break down the underlying patterns that lead to a high CV of SNa⁺ (i.e., oscillations vs. trends), to see how these relate to outcomes.

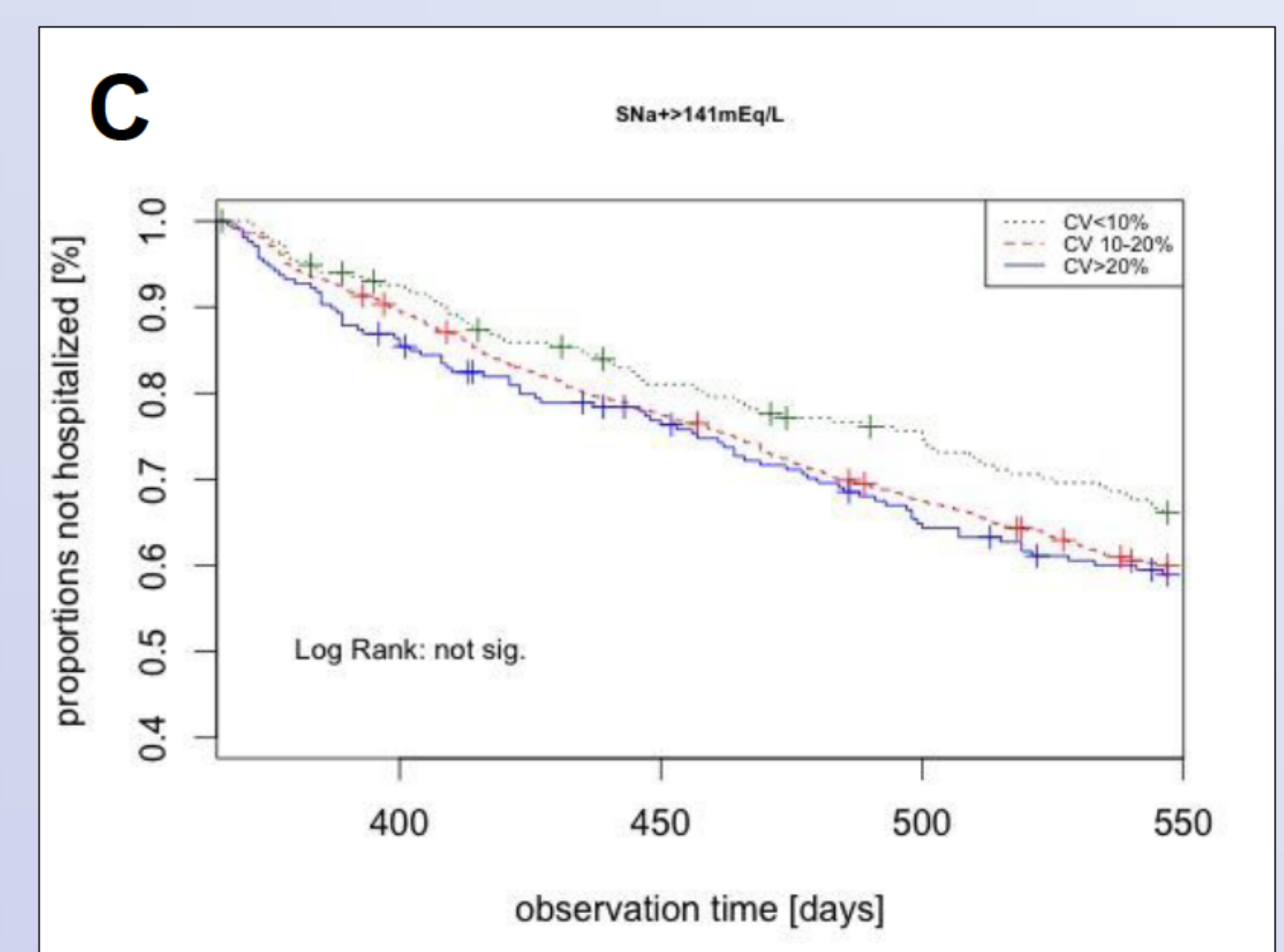
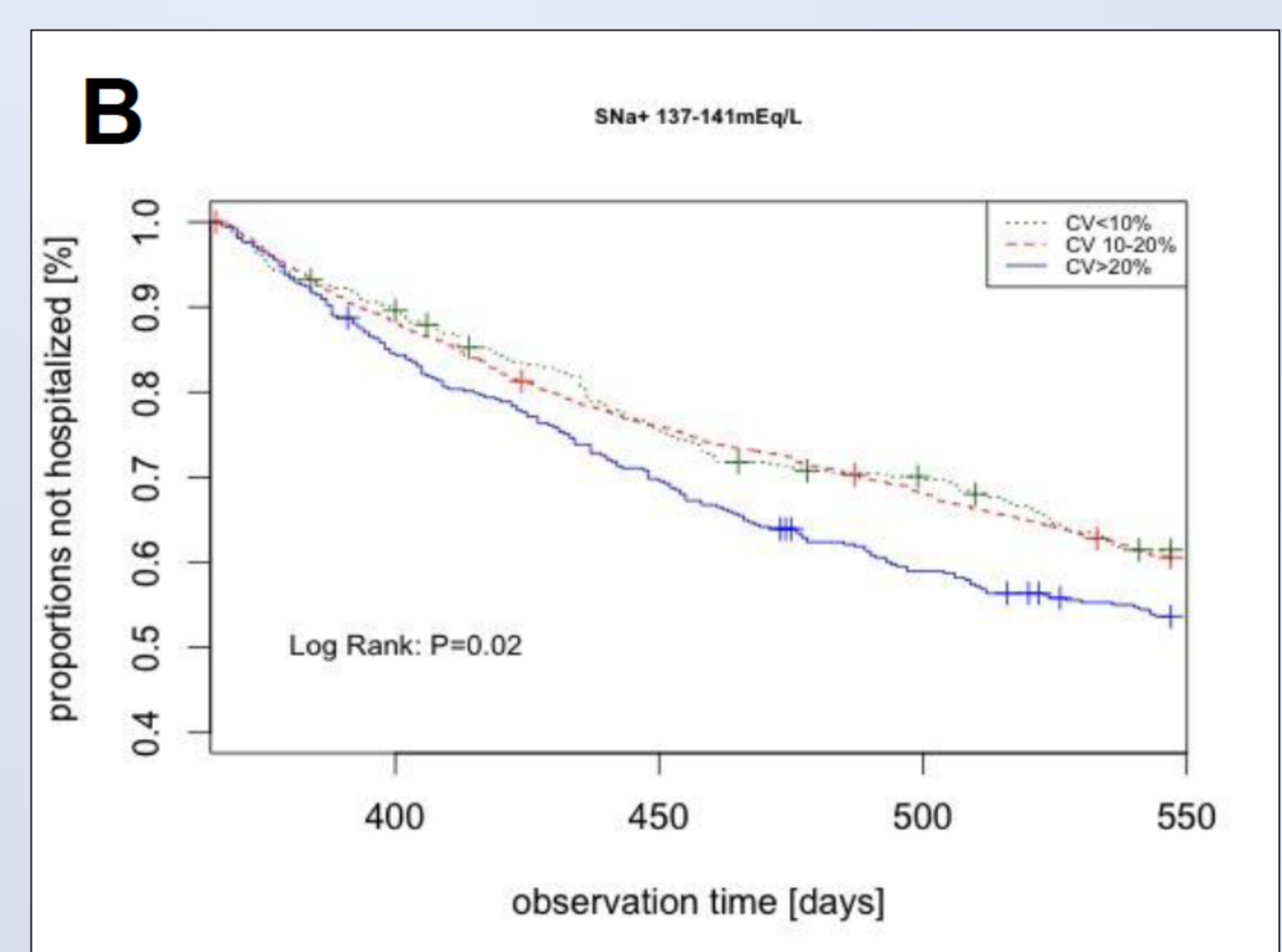
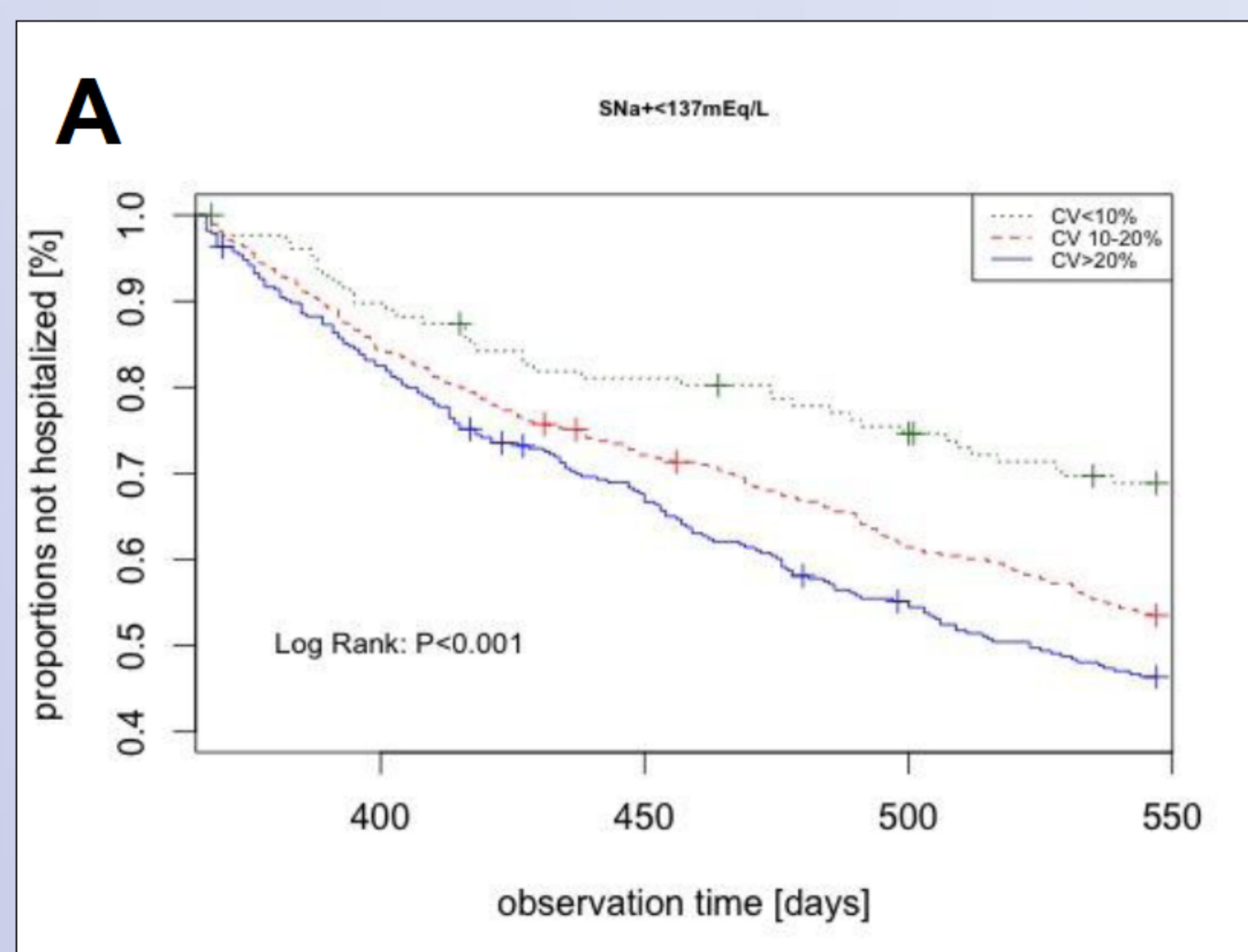


Figure 1: Kaplan Meier curves for time to first hospital admission during months 13 to 18. Patients are stratified by serum sodium (SNa⁺) and SNa⁺ variability (expressed as CV)

SNa ⁺ [mEq/L], CV SNa ⁺ (%)	Hazard Ratio (95% CI)
<137, <10	0.7 (0.5 to 1.1)
<137, 10-20	1.2 (0.9 to 1.5)
<137, >20	1.4 (1.1 to 1.7)
137-141, <10	reference
137-141, 10-20	1.0 (0.8 to 1.3)
137-141, >20	1.2 (1.0 to 1.5)
>141, <10	0.9 (0.7 to 1.2)
>141, 10-20	1.1 (0.9 to 1.3)
>141, >20	1.1 (0.8 to 1.5)

Table 1: Cox regression model for first hospital admission during months 13 to 18 by groups of SNa⁺ and SNa⁺ variability (expressed as CV).

