

# Hyperkalemia and angiotensin-converting enzyme inhibitor/angiotensin receptor neprilysin inhibitor titration in the era of sodium-glucose cotransporter 2 inhibitors

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**Introduction:** Angiotensin-converting enzyme inhibitors (ACEi) have been a key drug in treating heart failure with reduced (HF<sub>r</sub>EF) and mildly reduced ejection fraction (HF<sub>mr</sub>EF), with angiotensin receptor neprilysin inhibitors (ARNI) now proposed as a replacement. Guidelines recommend up-titrating these agents to the maximum tolerable dose for optimal benefit.<sup>1</sup> However, both ACEi and ARNI can increase potassium levels, leading to suboptimal dosing due to hyperkalemia concerns. Sodium-glucose cotransporter 2 inhibitors (SGLT2i) have been shown to reduce hyperkalemia risk in some patients. This study aimed to assess the prevalence of hyperkalemia in HF<sub>r</sub>EF and HF<sub>mr</sub>EF patients and its' effect on achieving optimal medical treatment.

**Patients and Methods:** This registry-based study included HF<sub>r</sub>EF and HF<sub>mr</sub>EF patients hospitalized at our center between September 2021 and December 2023. Levels above 4.7 mmol/L were considered as a cut-off for high potassium.

**Results:** A total of 764 HF<sub>r</sub>EF and HF<sub>mr</sub>EF patients were included, with 19.4% having HF<sub>mr</sub>EF and 80.6% HF<sub>r</sub>EF. The mean age was 68 years (range 27-90), and 73.3% were male. Potassium levels increased in 38.9% of patients after therapy implementation. 11.5% received the target doses of ACEi or ARNI. At therapy initiation, 22.8% had potassium levels  $\geq 4.7$  mmol/L. No significant association was found between potassium levels and the maximum ACEi/ARNI dose before SGLT2i use. Hyperkalemia prevented 2.4% of patients from receiving the maximum ACEi/ARNI dose. In HF<sub>mr</sub>EF, more patients were on medium to high ACEi doses at discharge compared to dose at admission. The most common reason for not achieving the maximum dose was low blood pressure or lack of regimen adherence.

**Conclusion:** In summary, while hyperkalemia impacted ACEi and ARNI dosing in a small portion of patients, it was not a major factor at inadequate therapy titration. Despite ACEi and ARNI raising potassium levels, factors like diuretic use and SGLT2i contributed to decrease in potassium levels in more patients.

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## LITERATURE

1. Delgado-Jiménez JF, Segovia-Cubero J, Almenar-Bonet L, de Juan-Bagudá J, Lara-Padrón A, García-Pinilla JM, et al. Prevalence, Incidence, and Outcomes of Hyperkalaemia in Patients with Chronic Heart Failure and Reduced Ejection Fraction from a Spanish Multicentre Study: SPANIK-HF Design and Baseline Characteristics. *J Clin Med.* 2022 Feb 22;11(5):1170. <https://doi.org/10.3390/jcm11051170>