

The use of beta-blockers for heart failure with reduced ejection fraction in the era of sodium-glucose transport protein 2 inhibitors

 Fran Rode^{1*},
 Ana Jordan¹,
 Ivan Zeljković¹,
 Nikola Pavlović¹,
 Ante Lisičić¹,
 Aleksandar Blivajs¹,
 Vanja Ivanović¹,
 Jelena Kursar¹,
 Danijela Grizelj¹,
 Luka Antolković¹,
 Domagoj Kobetić²,
 Ivan Skorić³,
 Šime Manola^{1,3},
 Ivana Jurin¹

¹Dubrava University Hospital, Zagreb, Croatia

²Pakrac General Hospital and the Croatian Veterans Hospital, Pakrac, Croatia

³University of Zagreb, School of Medicine, Zagreb, Croatia

RECEIVED:
October 13, 2024

ACCEPTED:
October 31, 2024



KEYWORDS: heart failure with reduced ejection fraction, beta-blockers, SGLT2 inhibitors.

CITATION: *Cardiol Croat.* 2024;19(11-12):435. | <https://doi.org/10.15836/ccar2024.435>

***ADDRESS FOR CORRESPONDENCE:** Fran Rode, Klinička bolnica Dubrava, Av. Gojka Šuška 6, HR-10000 Zagreb, Croatia. / Phone: +385-91-9440-330 / Email: fran.rode15@gmail.com

ORCID: Fran Rode, <https://orcid.org/0000-0002-8787-2455> • Ana Jordan, <https://orcid.org/0000-0001-5610-6259> • Ivan Zeljković, <https://orcid.org/0000-0002-4550-4056> • Nikola Pavlović, <https://orcid.org/0000-0001-9187-7681> • Ante Lisičić, <https://orcid.org/0000-0002-4365-9652> • Aleksandar Blivajs, <https://orcid.org/0000-0003-3404-3837> • Vanja Ivanović, <https://orcid.org/0000-0001-6931-5404> • Jelena Kursar, <https://orcid.org/0000-0001-8791-4910> • Danijela Grizelj, <https://orcid.org/0000-0002-8298-7974> • Luka Antolković, <https://orcid.org/0000-0002-5313-2213> • Domagoj Kobetić, <https://orcid.org/0009-0000-2106-4933> • Ivan Skorić, <https://orcid.org/0000-0002-5201-2092> • Šime Manola, <https://orcid.org/0000-0001-6444-2674> • Ivana Jurin, <https://orcid.org/0000-0002-2637-9691>

Introduction: Beta-blockers are one of the four major pillars of guideline-directed medical therapy (GDMT) for heart failure with reduced ejection fraction (HFrEF). The therapy has presented the best effects when up-titrated to evidence-based target doses. Despite their proven benefits, physicians have traditionally shown reluctance to up-titrate beta-blockers because of their negative inotropic and chronotropic effects. The effects of newly introduced sodium-glucose transporter 2 inhibitors (SGLT2I) in treating HFrEF might open more room for adequate beta-blockers up-titration¹. The goal of this study was to evaluate the up-titration practice, and impact of target doses of beta-blockers in patients with HFrEF receiving SGLT2I.

Patients and Methods: This is a prospective cohort study involving patients with HFrEF receiving SGLT2I therapy. Up-titration to the evidence-based targets was examined. We compared the groups of patients receiving maximally titrated beta-blockers versus incompletely titrated. Primary outcome was composite of: 1) rehospitalization or revisit to emergency unit due to the heart failure; 2) all-cause death and major adverse cardiac events (MACE). Secondary outcomes were heart rate at rest, left ventricular ejection fraction, NT-proBNP and New York Heart Association (NYHA) status at 6 and 12 months of follow-up. Study endpoints were documented via telephone interviews, regular outpatient follow-up, or by electronic hospital records.

Results: The study included 458 patients with median follow-up time of 365 (186-502) days. A total of 122 (26.6%) patients had maximally up-titrated beta-blockers. The results show adherence to maximal target doses of beta-blocker therapy significantly reduces hazard of death or MACE compared to not using maximal doses of beta-blocker (factor 0.43). Hazard reduction was not statistically significant for composite of rehospitalization or revisit to emergency unit due to HF. Maximal doses of beta-blockers did not result in a significant decrease in resting heart rate.

Conclusion: Our real-world data have highlighted the prevalence of incomplete titration of beta-blockers. Although it has been shown that evidence-based target dosing of beta-blockers reduce death and MACE, there is still room for improvement with up-titrating beta-blockers in eligible patients.

LITERATURE

1. Niriayo YL, Asgedom SW, Demoz GT, Gidey K. Treatment optimization of beta-blockers in chronic heart failure therapy. *Sci Rep.* 2020 Sep 28;10(1):15903. <https://doi.org/10.1038/s41598-020-72836-4>