













The role of C-reactive protein-albumin and red blood cell distribution width to albumin level ratio change in patients with heart failure in the sodium-glucose cotransporter-2 era

 **Marin Vidak**^{*},
 **Fran Šaler**¹,
 **Jasmina Čatić**¹,
 **Jelena Kursar**¹,
 **Petra Vitlov**¹,
 **Ana Šerman**²,
 **Miroslav Raguž**¹,
 **Diana Rudan**¹,
 **Andrej Novak**³,
 **Ivan Zeljković**¹,
 **Šime Manola**¹,
 **Ivana Jurin**¹

¹Dubrava University Hospital, Zagreb, Croatia

²University of Zagreb School of Medicine, Zagreb, Croatia

³University of Zagreb, Faculty of Science, Department of Physics, Zagreb, Croatia

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***ADDRESS FOR CORRESPONDENCE:** Marin Vidak, Klinička bolnica Dubrava, Avenija Gojka Šuška 6, HR-10000 Zagreb, Croatia. / Phone: +385-98-9011-876 / E-mail: marin.vidjak@gmail.com

ORCID: Marin Vidak, <https://orcid.org/0000-0003-0341-9598> • Fran Šaler, <https://orcid.org/0000-0002-1428-3940> • Jasmina Čatić, <https://orcid.org/0000-0001-6582-4201> • Jelena Kursar, <https://orcid.org/0000-0001-8791-4910> • Petra Vitlov, <https://orcid.org/0000-0001-6983-1409> • Ana Šerman, <https://orcid.org/0009-0007-8360-8466> • Miroslav Raguž, <https://orcid.org/0000-0003-1567-8503> • Diana Rudan, <https://orcid.org/0000-0001-9473-2517> • Andrej Novak, <https://orcid.org/0000-0002-7828-4870> • Ivan Zeljković, <https://orcid.org/0000-0002-4550-4056> • Šime Manola, <https://orcid.org/0000-0001-6444-2674> • Ivana Jurin, <https://orcid.org/0000-0002-2637-9691>

Introduction: Chronic inflammation plays a role in heart failure (HF) progression across its subtypes (reduced, mildly reduced, and preserved ejection fraction (EF)¹. While C-reactive protein (CRP) and albumin are known prognostic markers², the potential of the CRP-to-albumin ratio (CAR) and red blood cell distribution width-to-albumin ratio (RAR) as prognostic indicators in HF remains underexplored.

Patients and Methods: This prospective observational study was conducted at Dubrava University Hospital (CaRD registry, NCT06090591), enrolling HF patients between May 2021 and March 2024. Data on demographics, comorbidities, serum biomarkers, EF, and adverse events (death, HF-related emergencies, or hospitalizations) were collected. Patients with complete CRP and albumin measurements at baseline and 6-month follow-up were included.

Results: Among 1170 hospitalized HF patients, 368 were included. The median age was 67 years (IQR 60-74), 30% females (**Table 1**). Over the 6-month follow-up, CAR significantly decreased from 0.12 (95% CI 0.106-0.147) to 0.063 (95% CI 0.056-0.071), $p < 0.0001$, with no significant difference between empagliflozin and dapagliflozin groups ($p = 0.922$). There were 40 HF composite events. CAR and RAR were both correlated with HF composite events (CAR: $r = 0.163$, $p = 0.0017$; RAR: $r = 0.157$, $p = 0.0025$), particularly in the HFpEF group (CAR: $r = 0.32$, $p = 0.0032$; RAR: $r = 0.307$, $p = 0.0047$).

Conclusion: Sodium-glucose cotransporter-2 inhibitors (SGLT2i) significantly reduced CAR over the 6-month follow-up period, irrespective of the specific SGLT2i agent. Both CAR and RAR were independently associated with adverse HF outcomes, particularly in the HFpEF cohort, highlighting the significance of inflammatory processes in HF and the potential role of SGLT2i in modulating these markers in clinical practice.

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LITERATURE

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TABLE 1. Baseline characteristics of participants (n=386).

Category	Number	%
<i>Sex</i>		
Male	258	66.8
Female	110	28.5
<i>Dapagliflozin</i>		
Dapagliflozin	195	50.5
Empagliflozin	173	49.5
<i>NYHA status</i>		
NYHA I	15	3.9
NYHA II	174	45.1
NYHA III	156	40.4
NYHA IV	23	5.9
BMI (C, IQR)	28.5 (25.6-32.6)	
Smoking	128	33.1
<i>Comorbidities</i>		
Atrial fibrillation	171	44.3
Hypertension	302	78.2
Diabetes mellitus	158	40.9
Coronary artery disease	177	45.9
Peripheral artery disease	62	16.1
Dyslipidemia	256	66.3
Stroke / TIA	32	8.3
COPD / asthma	38	9.8
HFrEF	240	62.1
HFmrEF	45	11.7
HFpEF	83	21.5
<i>Ejection fraction</i>		
EF in HFrEF (C, IQR)	30 (25-35)	
EF in HFmrEF (C, IQR)	45 (43-46)	
EF in HFpEF (C, IQR)	55 (50-60)	
<i>Serum values</i>		
Hemoglobin (C, IQR)	138 (127-148.5)	
eGFR (C, IQR)	66.8 (49.9-84.6)	
NT-proBNP (C, IQR)	2612 (1143-6806)	
Albumin (C, IQR)	41 (38-43)	
CRP (C, IQR)	5 (2.1-11.35)	
RDW (C, IQR)	14.1 (13.4-15.2)	
CAR (C, IQR)	0.12 (0.05-0.28)	
RAR (C, IQR)	0.35 (0.32-0.4)	

NYHA = New York Heart Association functional classification, BMI = body mass index, C = median, IQR = interquartile range, TIA = transient ischemic attack, COPD = chronic obstructive pulmonary disease, EF = ejection fraction, HFrEF = heart failure with reduced ejection fraction, HFmrEF = heart failure with mildly reduced ejection fraction, HFpEF = heart failure with preserved ejection fraction, eGFR = estimated glomerular filtration rate, NT-proBNP = N-terminal prohormone of brain natriuretic peptide, CRP = C-reactive protein, RDW = red blood cell distribution width, CAR = C-reactive protein to albumin ratio, RAR = red blood cell distribution width to albumin ratio