

Systemic Inflammation and Its Association with Major Adverse Cardiovascular Events in Patients with Acute Myocardial Infarction

Chi Nguyen, PhD;¹ Amanda M. Ackermann, MD, PhD;¹ Erica Marieb, PhD;¹ Jeffrey R. Skaar, PhD;¹ Wing Chow, PharmD, MPH;¹ Radha Ryali, MS;¹ Lyuba Popadic;² Xiyuan Wu, MS;² Xinshuo Ma;² Michael J. Blaha, MD, MPH³

¹Novo Nordisk Inc., Plainsboro, NJ; ²Komodo Health, New York, NY; ³Johns Hopkins Ciccarone Center for the Prevention of Cardiovascular Disease, Baltimore, MD

Objectives

- To describe the demographic and clinical characteristics of patients with type 1 acute myocardial infarction (AMI), with and without systemic inflammation (SI).
- To assess the association of systemic inflammation with the risk of a major adverse cardiac event (MACE) or heart failure (HF) in patients with type 1 AMI

Introduction

- AMI is one of the leading causes of morbidity and mortality in the United States, with approximately 800,000 cases each year (600,000 first AMI, 200,000 recurrent).¹
- Despite the current standard of care, patients with AMI continue to have a high residual risk for future MACE.²
- AMI is associated with acute inflammation and chronic inflammation. Chronic systemic inflammation, whether occurring pre- or post-AMI, is associated with residual risk and poor prognosis.³
- Patients with AMI are at a higher risk of developing HF due to the structural and functional damage that occurs following the infarction. Previous studies indicate that about 20% to 30% of patients develop HF one year after discharge for AMI.⁴
- Clinical trials (CANTOS and LoDoCo2) showed that anti-inflammatory therapies (canakinumab and colchicine) significantly reduced cardiac events among patients with atherosclerotic cardiovascular disease.^{5,6}
- This study assessed the association of systemic inflammation with risk of recurrent or future MACE and incident HF in patients with type 1 AMI.

Methods

- This retrospective cohort study included adult patients hospitalized for a type 1 AMI from July 1, 2016 through December 31, 2023 (patient identification period).
- The study used the Komodo Healthcare Map database, including administrative claims, laboratory data, and mortality data. The index date was the first occurrence of type 1 AMI during the patient identification period.
- hsCRP test results within 1 year before or after an AMI admission determined chronic systemic inflammation status (with systemic inflammation, ≥ 1 hsCRP value 2-10 mg/L; without systemic inflammation, all hsCRP values < 2 mg/L).

Inclusion Criteria

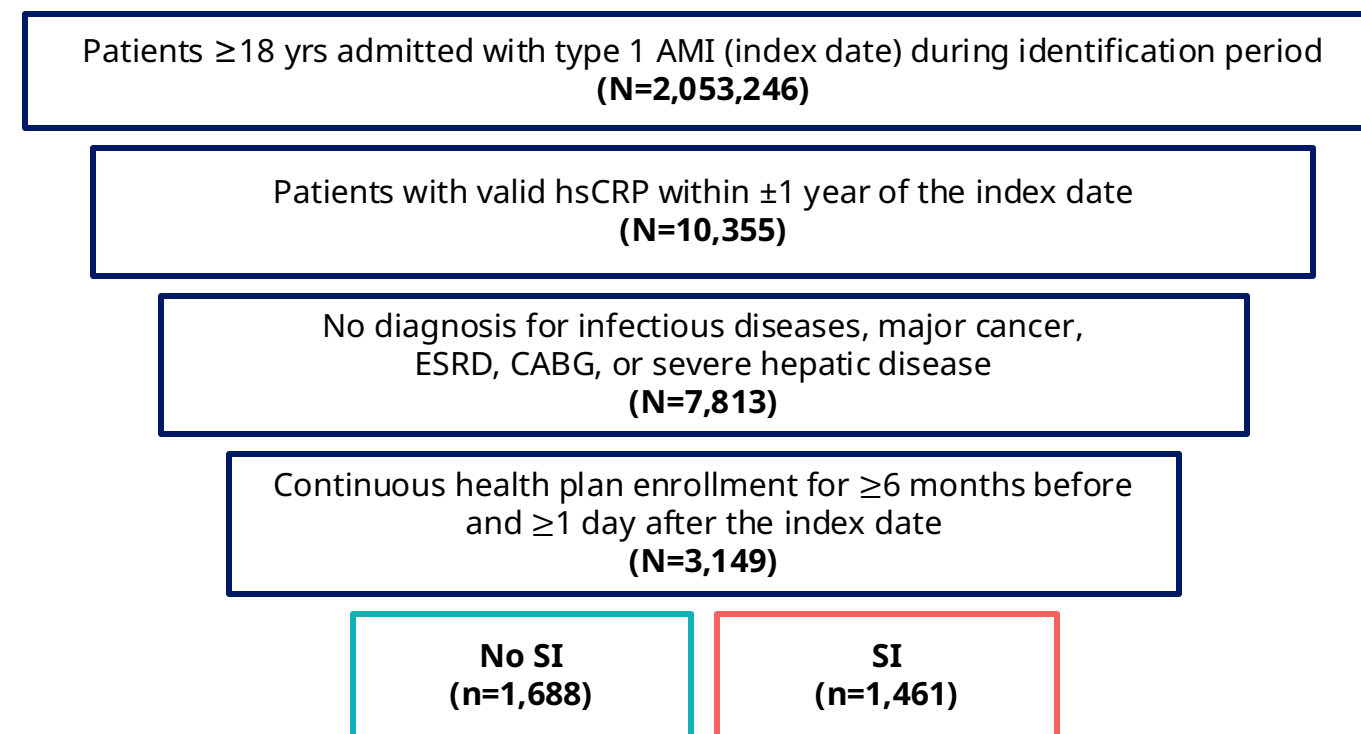
- Aged ≥ 18 years
- Inpatient admission of type 1 AMI, identified by International Classification of Diseases-10 diagnosis codes
- Continuous health plan enrollment for ≥ 6 months before and ≥ 1 day after index date

Exclusion criteria

- The following hsCRP tests were excluded as results would not be indicative of chronic systemic inflammation: tests within 30 days post-AMI; tests associated with antimicrobial, antiviral, or antimycotic use 2 weeks before or 1 week after the test date; tests with evidence of corticosteroid use during the 1 month before the test date; tests with values > 10 mg/L; or tests taken in inpatient or emergency department (ED) or within 30 days of inpatient/ED visit
- Patients with coronary artery bypass grafting (CABG) (at index), major cancer, end-stage renal disease (ESRD), severe hepatic disease, or chronic infectious disease (e.g., hepatitis, HIV)
- Descriptive statistics were reported for patient demographic and clinical characteristics at baseline.
- Incidence rates for composite endpoints of revised 3-point MACE (non-fatal MI, non-fatal stroke, or all-cause mortality) and revised 4-point MACE (non-fatal MI, non-fatal stroke, all-cause mortality, or urgent revascularization) and individual endpoints were estimated as the number of patients who experienced new events per 1,000 person-years (PY).
- For patients without prior HF, incidence rates of HF hospitalization and HF outpatient visits were estimated as the number of patients who developed HF per 1,000 PY.
- Cox proportional hazards models were used to examine the association between systemic inflammation and each outcome, adjusting for baseline characteristics.

Results

Figure 1: Patient selection flow chart



- A total of 3,149 patients with type 1 AMI were eligible for analysis (**Figure 1**). Among these, 1,461 (46.4%) had systemic inflammation, and 1,988 (74.2%) had no prior HF (regardless of systemic inflammation status).

Table 1: Patient baseline clinical characteristics

Characteristic	All patients with AMI with hsCRP test result (N=3,149)	AMI without SI (n=1,688)	AMI with SI (n=1,461)	P-value
Age, mean (SD)	61 (11)	60 (11)	61 (11)	0.07
Sex, n (%)				
Male	2,184 (69)	1,231 (73)	953 (65)	<0.01
Female	932 (30)	438 (26)	494 (34)	
Unknown	33 (1)	19 (1)	14 (1)	
Race, n (%)				<0.01
White	1,879 (60)	983 (58)	896 (61)	
Black/African American	242 (8)	113 (7)	129 (9)	
Asian/Pacific Islander	197 (6)	121 (7)	76 (5)	
Other	245 (8)	134 (8)	111 (8)	
Missing	586 (19)	337 (20)	249 (17)	
Payer type, n (%)				
Commercial	1,948 (62)	1,122 (66)	826 (57)	<0.01
Medicaid	871 (28)	418 (25)	453 (31)	
Medicare	330 (10)	148 (9)	182 (12)	
QCI, mean (SD)	0.62 (1.13)	0.51 (1.02)	0.75 (1.24)	<0.01
Categorical QCI*, n (%)				<0.01
0	2,143 (68)	1,238 (73)	905 (62)	
1	469 (15)	203 (12)	266 (18)	
2	308 (10)	151 (9)	157 (11)	
3+	229 (7)	96 (6)	133 (9)	
Prior MI*, n (%)	442 (14)	216 (13)	226 (15)	0.03
Prior PCI*, n (%)	73 (2)	40 (2)	33 (2)	0.80
Prior CABG*, n (%)	15 (1)	6 (<1)	9 (1)	0.30
hsCRP, mean (SD)	2.37 (2.29)	0.85 (0.47)	4.13 (2.29)	<0.01

*During the 6-month baseline

Abbreviations: AMI, acute myocardial infarction (type 1); PCI, percutaneous coronary intervention; CABG, coronary artery bypass grafting; hsCRP, high-sensitivity C-reactive protein; MI, myocardial infarction; QCI, Quan-Charlson Comorbidity Index; SD, standard deviation; SI, systemic inflammation

Patient Baseline Characteristics (Table 1, Figure 2)

- Compared to patients without systemic inflammation, patients with systemic inflammation were:
 - More likely to be female and to have more comorbid conditions, including hypertension (59% vs. 48%), dyslipidemia (58% vs. 51%), type 2 diabetes (34% vs. 22%), and prior MI (15% vs. 13%).
 - More likely to use medications, such as antihypertensives (60% vs. 51%) and immune suppressants (25% vs 20%).

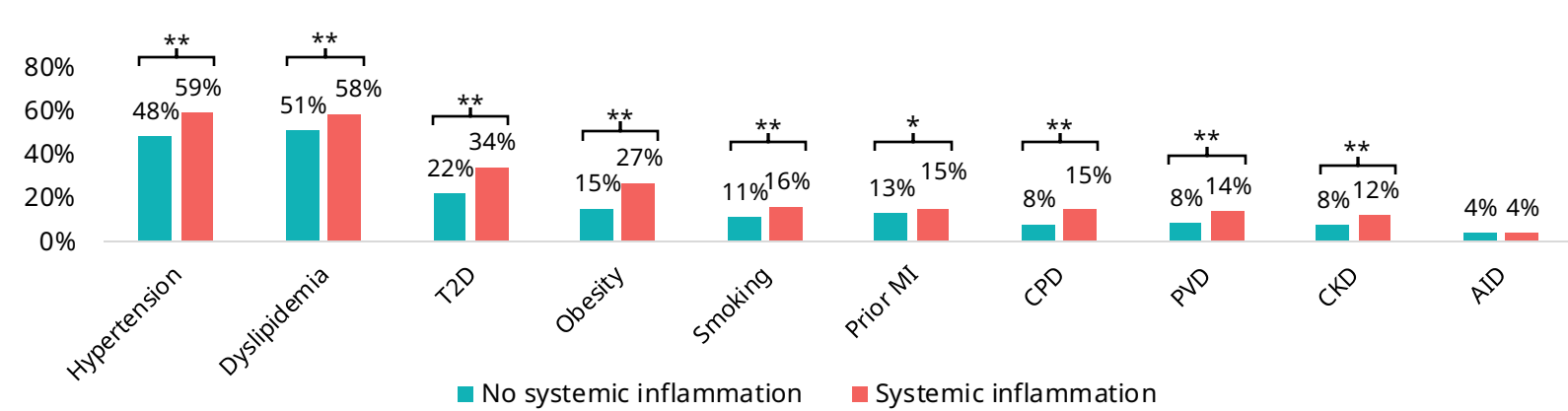
Revised 3- or 4-point MACE and Components (Table 2, Figure 4)

- The incidence rate of revised 3-point MACE was 45.4 (95% CI: 38.6-53.0) and 27.3 (95% CI: 22.5-32.7) per 1,000 PY for those with and without systemic inflammation, respectively.
- After controlling for baseline characteristics, systemic inflammation was associated with a 39% increase in the risk of revised 3-point MACE (HR: 1.39; 95% CI: 1.08-1.78) and a 26% increase in the risk of revised 4-point MACE (HR: 1.26; 95% CI: 1.01-1.58).
- In analyses of individual endpoints, systemic inflammation was associated with all-cause mortality (HR: 1.37; 95% CI: 1.07-1.75). Associations between systemic inflammation and non-fatal stroke (HR: 1.42; 95% CI: 0.72-2.79), non-fatal MI (HR: 1.16; 95% CI: 0.84-1.59), and urgent revascularization (HR: 0.90; 95% CI: 0.63-1.30) were not statistically significant.

Incident HF Among Patients Without Prior HF Diagnosis (Table 2, Figure 4)

- The incidence rate of HF hospitalization was 21.2 (95% CI: 15.6-28.2) and 9.5 (95% CI: 6.3-13.7) per 1,000 PY for patients with and without systemic inflammation, respectively.
- The incidence rate of HF outpatient visit was 71.0 (95% CI: 59.8-83.6) and 49.6 (95% CI: 41.5-58.7) per 1,000 PY for patients with and without systemic inflammation, respectively.
- After controlling for baseline characteristics, systemic inflammation was associated with HF hospitalization, corresponding to 104% increase in the risk of HF hospitalization (HR: 2.04; 95% CI: 1.26-3.30), but it was not significantly associated with HF outpatient visit (HR: 1.26; 95% CI: 0.99-1.61).

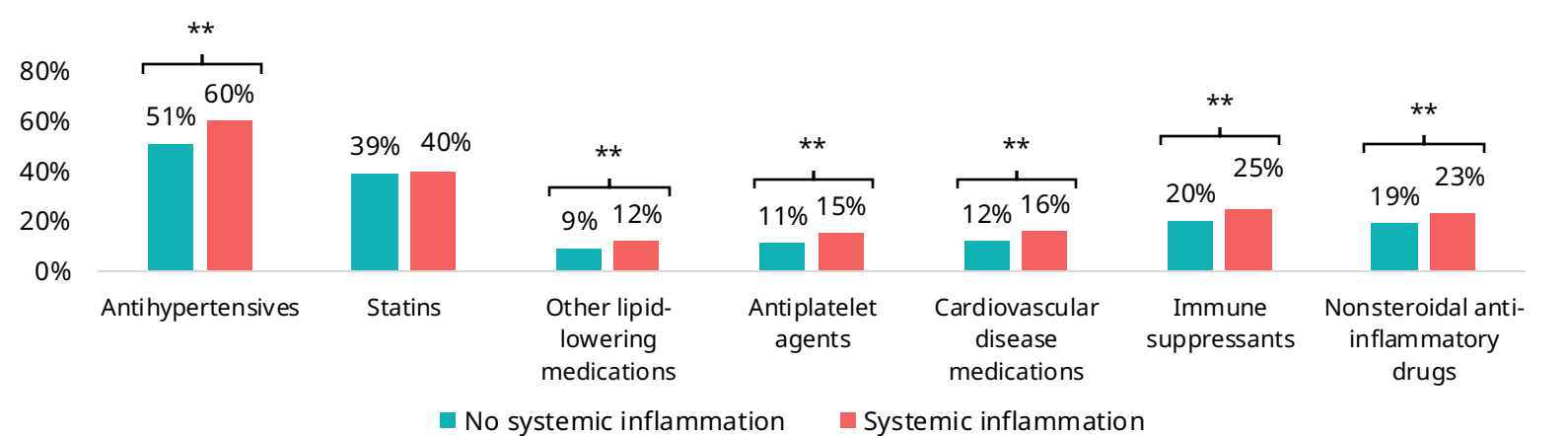
Figure 2: Patient comorbidities at baseline



*Significant difference between groups, $p < 0.05$; **Significant difference between groups, $p < 0.001$

Abbreviations: AID, autoimmune disease; CKD, chronic kidney disease; CPD, chronic pulmonary disease; MI, myocardial infarction; PVD, peripheral vascular disease; T2D, type 2 diabetes

Figure 3: Patient medication use at baseline

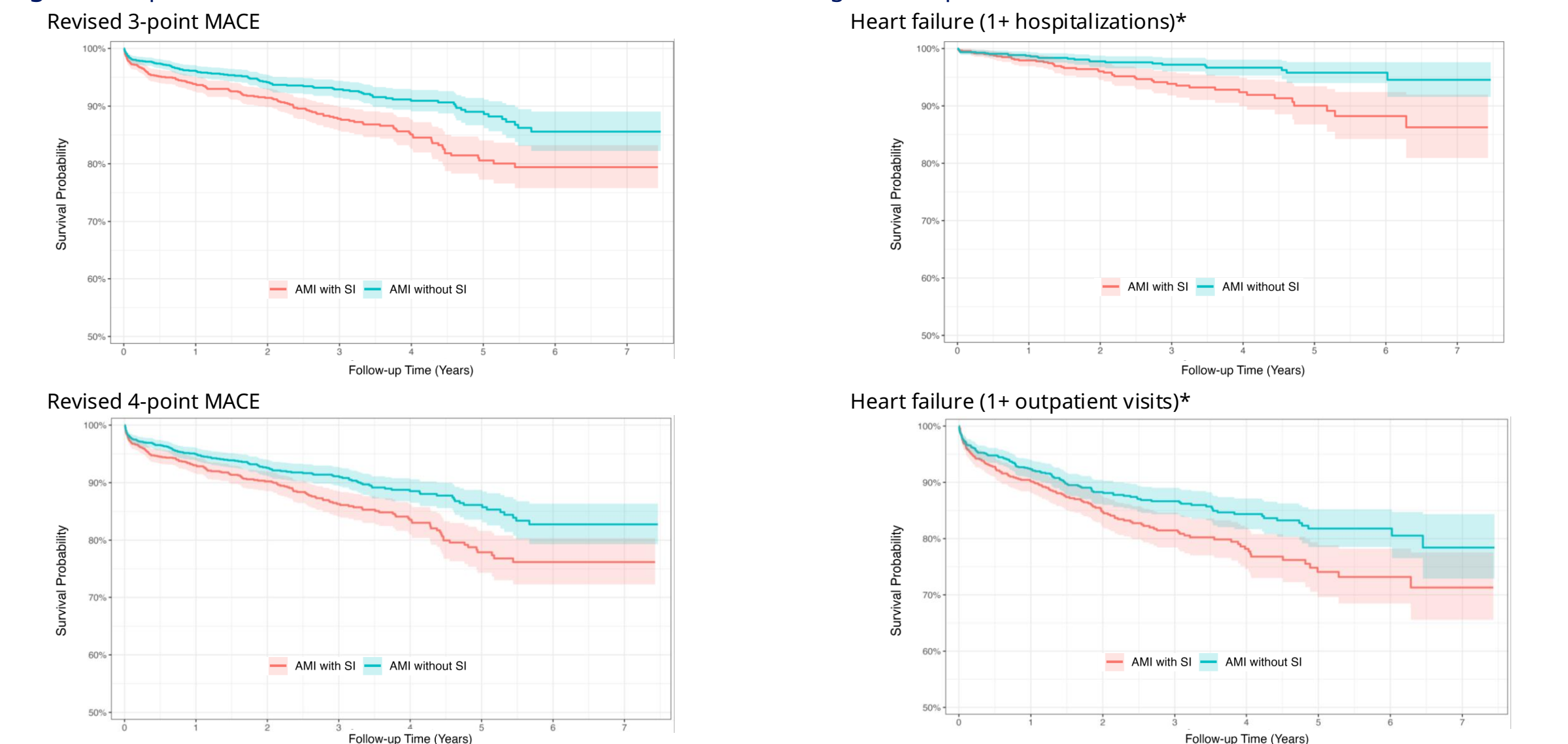


**Significant difference between groups, $p < 0.001$

Table 2: Association of systemic inflammation with individual and composite endpoints during follow-up

Outcome	Incidence rate (95% CI) per 1,000 person-years	Hazard ratio (95% CI)	Forest Plot
Revised 3-point MACE	27.3 (22.5 – 32.7)	45.4 (38.6 – 53.0)	1.39 (1.08 – 1.78)
Revised 4-point MACE	35.1 (29.6 – 42.3)	52.1 (44.8 – 60.3)	1.26 (1.01 – 1.58)
Non-fatal MI	17.9 (14.1 – 22.4)	24.5 (19.6 – 30.2)	1.16 (0.84 – 1.59)
Non-fatal Stroke	3.7 (2.1 – 6.0)	6.02 (3.8 – 9.1)	1.42 (0.72 – 2.79)
All-cause Mortality	7.5 (5.2 – 10.5)	14.9 (11.2 – 19.4)	1.37 (1.07 – 1.75)
Urgent Revascularization	16.2 (12.6 – 20.5)	15.7 (11.8 – 20.3)	0.90 (0.63 – 1.30)
HF (hospitalization or outpatient)*	51.6 (43.4 – 70.0)	72.8 (61.5 – 85.7)	1.26 (0.99 – 1.60)
HF (1+ hospitalizations)*	9.5 (6.3 – 13.7)	21.2 (15.6 – 28.2)	2.04 (1.26 – 3.30)
HF (1+ outpatient visits)*	49.6 (41.5 – 58.7)	71.0 (59.8 – 83.6)	1.26 (0.99 – 1.61)

Figure 4: Kaplan-Meier curves of MACE and incident HF outcomes during follow-up



Abbreviations: AMI, acute myocardial infarction; HF, heart failure; MACE, major adverse cardiac event; SI, systemic inflammation.

*HF outcomes were assessed among patients without prior HF.

Limitations

- This study was limited to patients with AMI who were tested for hsCRP with test results available; these patients may differ from the general population with AMI.
- Cardiovascular death could not be determined from the dataset, necessitating the use of all-cause death.
- The study population consisted of adults with US commercial insurance, Medicare, and Medicaid, which may limit the generalizability of the findings to the general US adult population.

Summary & Conclusions

- This retrospective cohort study found that systemic inflammation, defined by hsCRP levels 2-10 mg/L, was associated with unfavorable clinical outcomes in adult patients with recent type 1 AMI.
- The increased risks of revised 3-point MACE, revised 4-point MACE, and HF hospitalization among patients with AMI and systemic inflammation suggest substantial unmet clinical need in a population already receiving the standard of care.
- The findings suggest that hsCRP can inform risk assessment of future CV events in the setting of secondary prevention after type 1 AMI.

Disclosures: This study was funded by Novo Nordisk, Inc. CN, AA, EM, and JRS are employees of Novo Nordisk Inc. and shareholders of Novo Nordisk A/S. JS has equity in Trinity Life Sciences. WC and RR were employees of Novo Nordisk Inc. at the time the study was conducted. LP, XW, and XM are employees of Komodo Health, which was funded by Novo Nordisk Inc. to conduct this research. MB has received research grants, consulting fees or honoraria from the following commercial organizations: Novo Nordisk, Inc., Bayer Healthcare Pharmaceuticals, Inc., Idorsia, New Amsterdam, Novartis Corporation, Siemens, Aegle, Boehringer Ingelheim Pharmaceuticals, Inc., Merck & Co, Inc. and Vectura. MB has received research grants, consulting fees or honoraria from the following non-commercial organizations: American College of Cardiology, American Heart Association, The Food and Drug Administration, and the National Institutes of Health. The authors acknowledge the contributions of Kathleen Kearney, MD, to this work and the medical writing support of Benjamin Doty, PhD, of KJT Group, Inc. funded by Novo Nordisk Inc. in accordance with Good Publication Practice (GPP) guidelines.

Presented at AMCP 2026, Nashville, TN, April 13-16, 2026.

References:

- Tsoo CW, Aday AW, Almaraz-Zoo L, et al. Heart Disease and Stroke Statistics - 2023 update: a report from the American Heart Association. *Circulation*. 2023;147(8):e93-e621.
- Dhinda DS, Sandesara PB, Shapiro MD, Wong ND. The evolving understanding and approach to residual cardiovascular risk management. *Front Cardiovasc Med*. 2020;7:88.
- Arnold N, Lechner K, Waldeyer C, Shapiro MD, Koenig W. Inflammation and cardiovascular disease: the future. *Eur Cardiol*. 2021;16:e20.
- Jenča D, Melenovský V, Stehlik J, et al. Heart failure after myocardial infarction: incidence and predictors. *ESC Heart Fail*. 2021;8(1):222-237. doi:10.1002/ehf2.13144.
- Ridker PM, Everett BM, Thuren T, et al.; CANTOS Trial Group. Antiinflammatory therapy with canakinumab for atherosclerotic disease. *N Engl J Med*. 2017;377(12):1119-1131.
- Nidorf SM, Fiolet ATL, Mosterd A, et al.; LoDoCo2 Trial Investigators. Colchicine in patients with chronic coronary disease. *N Engl J Med*. 2020;383(19):1838-1847.