EPH162

Real-World Demographic and Clinical Characteristics of Patients With Atherosclerotic Cardiovascular Disease With or Without Chronic Kidney Disease or Systemic Inflammation in the United States

Chi Nguyen, PhD[1]; Allegra Kaufman, MD[1]; Brenna Brady, PhD[2]; Ryan Ross, MS[2]; Wing Chow, PharmD, MPH[1]; Aarth Sheth, PharmD, RPh[1]; Radha Ryali, MS[1]; Weilong Li, PhD[1]; Jeffrey R Skaar, PhD[1]

Background & Aim

Cardiovascular disease affects ~10% of US adults (28.6 million), contributing to ~4.7 million hospitalizations in 2021 and 941,652 deaths in 2022.[1]

Clinical studies support the hypothesis that systemic inflammation (SI) plays a critical role in atherosclerotic cardiovascular disease (ASCVD)

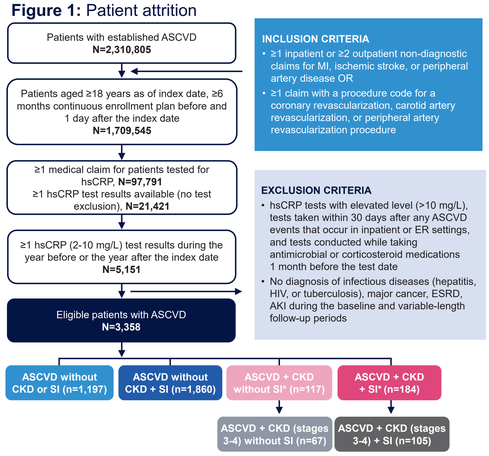
- The CANTOS clinical trial demonstrated that anti-inflammatory therapy significantly reduced adverse cardiac events in patients with established ASCVD and elevated high-sensitivity C-reactive protein (hsCRP) levels[2]
- Among patients receiving statin therapy, a collaborative analysis of 3 trials reported that hsCRP was significantly associated with major adverse cardiovascular events (MACE)[3]
- Among patients intolerant to statin therapy, the CLEAR outcomes trial reported that baseline hsCRP was significantly associated with MACE[4]

This study describes demographic and clinical characteristics and MACE in patients with ASCVD ± chronic kidney disease (CKD), with or without SI.

Methods

- This retrospective cohort study used the Merative™ MarketScan® Research Database claims (commercial, Medicare, and laboratory) from October 2015–December 2022 and identified patients between October 2016–September 2022; the first claim for ASCVD during this period was set as the index date (diagnosis date)
- Presence of ASCVD was identified using the International Classification of Diseases, 10th Revision, Clinical Modification (ICD-10-CM) diagnosis, ICD-10 procedure, and Current Procedural Terminology (CPT) codes (**Figure 1**)
- Patients with CKD were identified based on ICD-10 diagnosis codes or estimated glomerular filtration rate (eGFR)
  - For CKD, ≥1 medical claim or ≥2 laboratory test results for eGFR indicating CKD <60 mL/min/1.73 m^2 that were ≥90 days apart
  - For stages 3-4 CKD, ≥1 medical claim or ≥2 laboratory test results for eGFR indicating CKD between 15-60 mL/min/1.73 m^2 that were ≥90 days apart
- Presence of SI was determined using hsCRP laboratory data in the 1 year before or after the index date. The hsCRP test result closest to the index date was used. Patients whose hsCRP test result was ≥2 mg/L were considered to have SI
- Baseline demographics and clinical characteristics were described using descriptive statistics
- Incidence rates (per 1,000 person-years) were reported for a composite of non-fatal myocardial infarction (MI) and non-fatal stroke (2-point MACE)
- A Cox proportional hazard model was used to examine the risks of 2-point MACE while controlling for patient baseline characteristics

Figure 1: Patient attrition



*The cohort ASCVD+CKD±SI included CKD stages 1-5. AKI, acute kidney injury; ASCVD, atherosclerotic cardiovascular disease; CKD, chronic kidney disease; CPT, Current Procedural Terminology; ER, emergency room; ESRD, end-stage renal disease; hsCRP, high-sensitivity C-reactive protein; MI, myocardial infarction; SI, systemic inflammation

Results

- Among 3,358 eligible patients with ASCVD (**Table 1**)
  - 54% were male, and the mean age was 60 years
  - 30.5% were insured by Medicare Advantage or Medicare Supplemental plan
- Among eligible patients with ASCVD, 61% (n=2,044) of patients had SI
  - 67% of females had SI
  - 56% of males had SI
  - Patients with and without SI had a similar mean age
- Among eligible patients with ASCVD, 9% (n=301) of patients had CKD; 5% (n=172) had stages 3-4 CKD
  - Mean age of patients with CKD was ≥9 years higher (≥11 years for stages 3-4 CKD) than patients without CKD
  - Patients with and without SI were of similar age in the CKD subsets

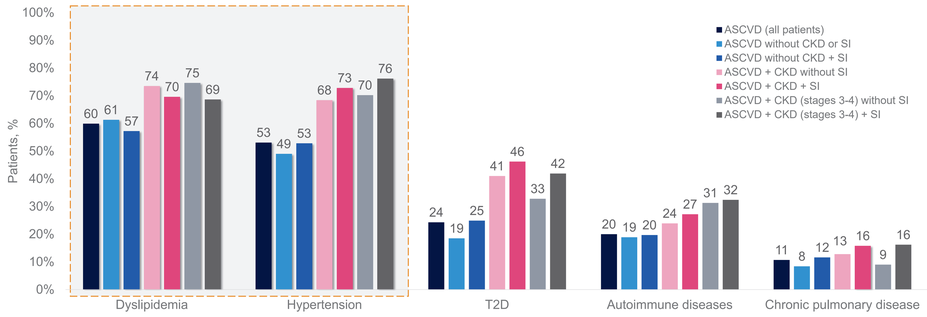
Table 1: Patient baseline demographic characteristics and hsCRP level

	ASCVD N=3,358	ASCVD without CKD or SI n=1,197	ASCVD without CKD + SI n=1,860	ASCVD + CKD without SI n=117	ASCVD + CKD + SI n=184	ASCVD + CKD (stages 3-4) without SI n=67	ASCVD + CKD (stages 3-4) + SI n=105
Age, mean (SD), y	60.2 (11.8)	59.6 (11.0)	59.2 (11.7)	69.1 (12.5)	68.8 (11.3)	72.7 (12.0)	70.9 (11.0)
Sex, n (%)							
Male	1,814 (54.0)	737 (61.6)	917 (49.3)	69 (59.0)	91 (49.5)	33 (49.3)	51 (48.6)
Female	1,544 (46.0)	460 (38.4)	943 (50.7)	48 (41.0)	93 (50.5)	34 (50.8)	54 (51.4)
Insurance type, n (%)							
Commercial	2,334 (69.5)	868 (72.5)	1,350 (72.6)	47 (40.2)	69 (37.5)	19 (28.4)	34 (32.4)
Medicare	1,024 (30.5)	329 (27.5)	510 (27.4)	70 (59.8)	115 (62.5)	48 (71.7)	71 (67.6)
Geographic region, n (%)							
Northeast	869 (25.9)	309 (25.8)	502 (27.0)	20 (17.1)	38 (20.7)	12 (17.9)	21 (20.0)
North Central	806 (24.0)	277 (23.1)	416 (22.4)	47 (40.2)	66 (35.9)	33 (49.3)	38 (36.2)
South	1,315 (39.2)	470 (39.3)	736 (39.6)	42 (35.9)	67 (36.4)	22 (32.8)	39 (37.1)
West	367 (10.9)	141 (11.8)	205 (11.0)	*	13 (7.1)	0 (0.0)	*
Other	*	0 (0.0)	*	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
hsCRP, mean (SD), mg/L	3.2 (2.2)	1.4 (0.3)	4.4 (2.1)	1.4 (0.3)	4.4 (2.1)	1.4 (0.3)	4.5 (2.2)

*Indicates that the number of patients is 1-9. ASCVD, atherosclerotic cardiovascular disease; CKD, chronic kidney disease; hsCRP, high-sensitivity C-reactive protein; SD, standard deviation; SI, systemic inflammation

- Dyslipidemia (60%), hypertension (53%), and type 2 diabetes (T2D, 24%) were common comorbidities for the overall ASCVD study population (**Figure 2**)
  - Hypertension (73%), dyslipidemia (70%), and T2D (46%) were the most common comorbidities in patients with ASCVD+CKD+SI

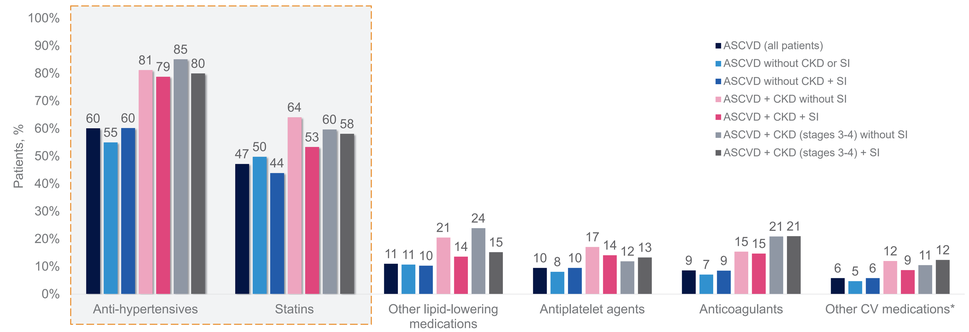
Figure 2: Patient baseline comorbidities



ASCVD, atherosclerotic cardiovascular disease; CKD, chronic kidney disease; SI, systemic inflammation; T2D, type 2 diabetes

- In the overall study population with ASCVD, anti-hypertensives (60%) and statins (47%) were the most common medications used at baseline, followed by other lipid-lowering (11%), anti-platelet (10%), and anti-coagulant (9%) medications (**Figure 3**)
  - In patients with ASCVD+CKD, anti-hypertensives (81% without SI, 79% +SI) and statins (64% without SI, 53% +SI) were the most prescribed medications
  - For patients with CKD (stages 3-4), anti-hypertensives (85% without SI, 80% +SI) and statins (60% without SI, 58% +SI) were the most prescribed medications

Figure 3: Patient baseline medication use



*Other CV medications include digitalis preparation, thrombolytic, vasodilators. ASCVD, atherosclerotic cardiovascular disease; CKD, chronic kidney disease; CV, cardiovascular; SI, systemic inflammation

- The incidence rate for 2-point MACE for the overall population with ASCVD was 9.5 per 1,000 person-years (95% CI, 7.5–11.9; **Table 2**)

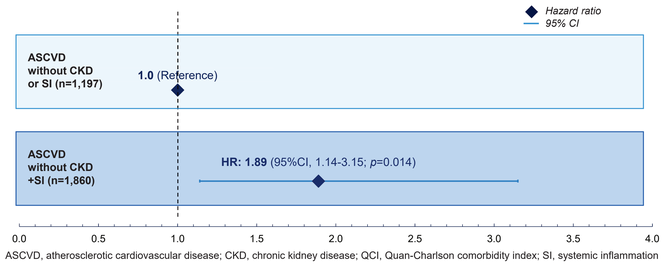
Table 2: Incidence rate for 2-point MACE*

	ASCVD N=3,358	ASCVD without CKD or SI n=1,197	ASCVD without CKD + SI n=1,860	ASCVD + CKD without SI n=117	ASCVD + CKD + SI n=184	ASCVD + CKD (stages 3-4) without SI n=67	ASCVD + CKD (stages 3-4) + SI n=105
Incidence rate per 1,000 person-years	9.5	7.0	12.0	3.3	6.1	5.4	7.2
95% CI	7.5–11.9	4.3–10.7	9.0–15.7	0.1–18.6	1.3–17.8	0.1–30.0	0.9–25.8

*Events occurring on the index date were excluded, and a follow-up event after index discharge was captured if present. ASCVD, atherosclerotic cardiovascular disease; CKD, chronic kidney disease; SI, systemic inflammation

- Among patients with ASCVD without CKD, for whom we have a sufficient sample size for the Cox proportional hazards model, SI was associated with an increased risk of 2-point MACE (adjusted HR=1.89; 95% CI, 1.14–3.15; p=0.014; **Figure 4**)
  - Due to the small sample size and number of events for patients with CKD or CKD stages 3-4, no conclusion regarding 2-point MACE can be drawn

Figure 4: Time to first 2-point MACE, Cox proportional hazards model (controlled for age, sex, and QCI)



ASCVD, atherosclerotic cardiovascular disease; CKD, chronic kidney disease; QCI, Quan-Charlson comorbidity index; SI, systemic inflammation

Discussion and Conclusion

- In the overall population with ASCVD, dyslipidemia, hypertension, and T2D were common comorbidities
- Over half (61%) of patients with ASCVD exhibited SI
  - SI was more common among females and was associated with an increased risk of 2-point MACE in patients without CKD
- A larger sample size of patients with ASCVD+CKD is needed for future assessment of MACE
  - In patients with CKD or CKD stages 3-4, the wide range of 95% CI for 2-point MACE incidence rate is attributed to the small sample sizes, indicating a need for further research on MACE in these patient populations
- A higher proportion of patients with CKD versus without CKD received anti-hypertensives and statins, medications that can reduce hsCRP levels.[5,6] It is possible that treatment with these medications reduced the risk of MACE in patients with CKD
- Limitation: Patients with CKD and CKD stages 3-4 were identified using diagnosis and laboratory values and were likely under-coded in claims data, resulting in small sample sizes. Additionally, eGFR data were available for only a subset of patients
- **Conclusion:** Patients with ASCVD should be monitored for common comorbidities and SI, and the risk of MACE should be considered in treatment planning and optimization

Author Affiliations
[1]Novo Nordisk, Inc., Plainsboro, NJ, USA
[2]Merative, Ann Arbor, MI, USA

Presented at ISPOR 2025, Montreal, QC, Canada, May 13-16, 2025

Disclosures
- This research was funded by Novo Nordisk Inc (Plainsboro, NJ, USA).
- Medical writing and editorial support was provided by Meggha Dave, MPharm, and Laura McCormick, PhD, of KJT Group, Inc. (Rochester, NY, USA), funded by Novo Nordisk Inc.
- CN, AK, WC, AS, RR, WL, and JS are employees and shareholders of Novo Nordisk Inc. JS is an equity holder in Trinity Life Sciences.
- BB and RR are employed by Merative, a consulting company that has received funding from Novo Nordisk to carry out this research.

Abbreviations
AKI, acute kidney injury; ASCVD, atherosclerotic cardiovascular disease; CKD, chronic kidney disease; CPT, Current Procedural Terminology; CRP, C-reactive protein; CVD, cardiovascular disease; ER, emergency room; ESRD, end-stage renal disease; hsCRP, high-sensitivity C-reactive protein; ICD-10-CM, International Classification of Diseases, Tenth Revision, Clinical Modification; MACE, major adverse cardiovascular events; MI, myocardial infarction; SD, standard deviation; SI, systemic inflammation; T2D, type 2 diabetes.

References:
(**1**) Martin SS, Aday AW, Allen NB, et al. 2025 Heart Disease and Stroke Statistics: A Report of US and Global Data From the American Heart Association. Circulation. 2025; 151:e41–e660.
(**2**) Ridker PM, Everett BM, Thuren T, et al. Anti-inflammatory therapy with canakinumab for atherosclerotic disease. N Engl J Med. 2017;377(12):1119-1131.
(**3**) Ridker PM, PM, Bhatt DL, Pradhan AD, et al. Inflammation and cholesterol as predictors of cardiovascular events among patients receiving statin therapy: a collaborative analysis of three randomised trials. Lancet. 2023;401(10384):1293-1301.
(**4**) Ridker PM, Lei L, Louie MJ, et al. Inflammation and cholesterol as predictors of cardiovascular events among 13 970 contemporary high-risk patients with statin intolerance. Circulation. 2024;149(1):28-35.
(**5**) Kim-Mitsuyama S, Soejima H, Yasuda O, et al. Reduction in hsCRP levels is associated with decreased incidence of cardiovascular events in Japanese hypertensive women but not in men. Sci Rep. 2020;10(1):17040.
(**6**) Ridker PM, Cannon CP, Morrow D, et al. C-reactive protein levels and outcomes after statin therapy. N Engl J Med. 2005;352(1):20-28.