Association between High-Intensity Statin Adherence and Cholesterol Reduction in Veterans with Chronic Kidney Disease

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BACKGROUND

- Chronic kidney disease (CKD) affects 30 million adults in the U.S.[1]
- CKD = cardiovascular risk equivalent
- Role of statin therapy is well-established in primary/secondary prevention of atherosclerotic cardiovascular disease (ASCVD)

Atorvastatin[2]
- Extensively metabolized via liver
- No renal adjustments

Rosuvastatin[3]
- Not extensively metabolized via liver
- Increased concentrations in renal impairment
- Should not exceed 10mg/day in severe CKD

Ford and Colleagues[4] (2007)
- Randomized control trial evaluating 6595 men receiving pravastatin versus placebo for primary prevention
- < 40% patients receiving statin continued therapy 5 years after study end

Rodriguez and colleagues[5] (2019)
- Retrospective cohort including 347,104 patients receiving statins at Veteran Affairs sites
- Primary outcome: death from all causes
- Compared to medication possession ratio (MPR) ≥ 90%
  - MPR < 50%: HR of 1.3 (95% CI, 1.27-1.34)
  - MPR 50-69%: HR of 1.21 (95% CI, 1.18-1.24)
  - MPR 70-89%: HR of 1.08 (95% CI, 1.06-1.09)

American College of Cardiology/ American Heart Association (ACC/AHA) Guidelines[6,7]
- Patient-specific factors
- 10-year ASCVD risk score or established ASCVD
- 2013: Statin benefit groups
- 2018: Risk discussions/ risk enhancers
- High-intensity indicated for select patients regardless of CKD status

- A systematic review estimated medication nonadherence varying from 17-74% among patients with CKD[8]
- Limited evidence regarding impact of adherence rates to high-intensity statins in patients with renal impairment

OBJECTIVES

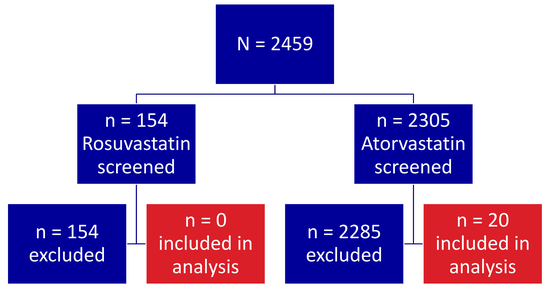
- The primary outcome was to evaluate the relationship between high-intensity statin adherence (MPR ≥ 80%) versus high-intensity statin nonadherence (MPR < 80%) and LDL-c reduction
- The secondary outcome was to assess the safety of high-intensity statins in patients demonstrating adherence versus nonadherence on the basis of adverse events and liver enzyme abnormalities

METHODS

Inclusion Criteria	Exclusion Criteria
• Age ≥ 40 and ≤ 75 years with T2DM and LDL-c 70 to 189 mg/dL • Age ≥ 18 years with LDL-c ≥ 190 mg/dL • Established ASCVD (ischemic heart disease, cerebrovascular disease, and PVD) • New user of high-intensity statin (6-month statin-free period)	• eGFR > 60 mL/min/1.73m^2 or < 15 mL/min/1.73m^2 • Concurrent non-statin lipid lowering therapy • Switched statins during study • Admitted for more than 30 consecutive days • Non-VA statin medication • New diagnosis of ASCVD within 1 month of statin initiation

- Retrospective chart review
- Study period: 11/01/2013 – 08/31/2018
- Setting: VA North Texas Health Care System
- Medication prescribing practices included:
  - Atorvastatin 40 mg or 80 mg daily
  - Rosuvastatin 20 mg or 40 mg daily
- MPR per refill history in CPRS
  - Adherence (≥ 80%) versus nonadherence (< 80%)
- Statistical analysis: Wilcoxon rank-sum test and Fisher's exact test

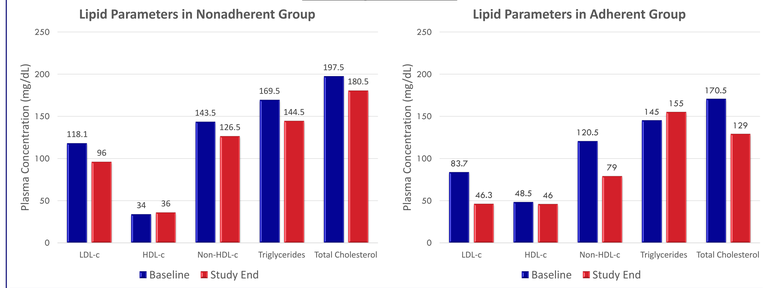
RESULTS



Baseline Characteristic	Nonadherent (n = 10)	Adherent (n = 10)	P-Value
Medication Possession Ratio, %; median (IQR)	69 (63, 70)	88 (85, 92)	< 0.001
Age, years; median (IQR)	66 (57, 74)	68 (62, 71)	0.85
Male, %	100	100	0.85
Race, %			0.48
White/Caucasian	50	70	--
Black/African American	40	20	--
Native Hawaiian/Declined to Answer	10	10	--
Statin Benefit Group, %			--
T2DM and LDL-c 70-189 mg/dL	40	40	--
Established ASCVD	60	60	--
Mean Atorvastatin Dose, mg	40	40	--
eGFR, mL/min/1.73m^2; median (IQR)	47 (42, 53)	40.5 (32, 51)	0.4
LDL-c, mg/dL; median (IQR)	118.1 (102.2, 156.4)	83.7 (79.2, 106)	0.02
HDL-c, mg/dL; median (IQR)	34 (23, 34)	48.5 (44, 52)	0.006
Non-HDL-c, mg/dL; median (IQR)	143.5 (134, 186)	120.5 (111, 147)	0.09
Triglycerides, mg/dL; median (IQR)	169.5 (136, 288)	145 (108, 172)	0.23
Total Cholesterol, mg/dL; median (IQR)	197.5 (171, 219)	170.5 (156, 188)	0.13
AST, U/L; median (IQR)	19.5 (17, 32)	23.5 (21, 24)	0.32
ALT, U/L; median (IQR)	18.5 (13, 28)	24.5 (16, 32)	0.45

RESULTS

Primary Outcome



Change in Plasma Concentrations of Lipids	Nonadherent (n = 10)	Adherent (n = 10)	P-Value
LDL-c, mg/dL; median (IQR)	-22.1 (-48, -9.6)	-37.4 (-42.6, 8.8)	0.88
HDL-c, mg/dL; median (IQR)	2 (-2, 5)	-2.5 (-7, 0)	0.16
Non-HDL-c, mg/dL; median (IQR)	-17 (-52, -10)	-41.5 (-73, -2)	0.94
Triglycerides, mg/dL; median (IQR)	-25 (-75, 37)	10 (-52, 34)	0.55
Total Cholesterol, mg/dL; median (IQR)	-17 (-47, -2)	-41.5 (-61, 8)	0.76

Secondary Outcome

Adverse Effects	Nonadherent (n = 10)	Adherent (n = 10)	P-Value
AST, U/L; median (IQR)	2.5 (-2, 3)	0 (-3, 2)	0.36
ALT, U/L; median (IQR)	0.5 (-1, 4)	-0.5 (-10, 3)	0.54
Reported adverse effects	0	0	--

DISCUSSION

Strengths
- Evaluated patients with CKD
- Use of medication possession ratio versus prescriber records

Limitations
- Small sample size
- Formulary restrictions
- 2018 ACC/AHA Cholesterol Guidelines

Future Direction
- Extending study date for inclusion of rosuvastatin (formulary update)
- Data expansion to more VA sites
- Time-to-event analyses

CONCLUSIONS

In patients with CKD and receiving high-intensity atorvastatin, there was no significant difference in lipid parameters and safety outcomes between nonadherent and adherent groups. The impact of compliance with high-intensity rosuvastatin in patients with CKD and resulting lipid parameters remains unclear.

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Disclosure Statement: Authors of this presentation have nothing to disclose concerning possible financial or personal relationships with commercial entities that may have a direct or indirect interest in the subject matter of this presentation.