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Association of Low-Density Lipoprotein Testing after an Atherosclerotic Cardiovascular Event with Subsequent Statin Adherence and Intensification

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Abstract

Purpose: Evaluate associations between outpatient low-density lipoprotein cholesterol (LDL-C) testing and subsequent statin adherence and intensification in patients after an atherosclerotic cardiovascular (ASCVD) event.

Methods—Longitudinal study of adult members of Kaiser Permanente Northern California hospitalized with an ASCVD event (myocardial infarction or stroke) during 01/01/2016 to 12/31/2017 with follow-up through 12/31/2019. Outcomes were statin adherence (estimated using continuous medication gap (CMG)) and intensification (defined by an increased dose or switch to a higher-intensity statin) based on pharmacy dispensing. The exposure of interest was first outpatient LDL-C test after an ASCVD event. Baseline for follow-up was LDL-C test date or a date assigned using incidence density sampling. Multivariate logistic regression models were specified to estimate the odds ratios (OR) for statin adherence or intensification among those with

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versus without an LDL-C test, with adjustment for age, sex, race/ethnicity, smoking, hypertension, diabetes, BMI and eGFR.

Results—There were 19,604 adults hospitalized with ASCVD including 7,054 adults not on high-intensity statins; mean age was 69.5 years and 33.0% were women. Prevalence of good adherence (CMG≤20%) was significantly higher (80.2% vs 75.9%; OR=1.38; 95% CI: 1.28, 1.49; p<.001) among participants who had an LDL-C test compared to participants who did not. LDL-C testing was associated with significantly higher rates of treatment intensification (16.1% vs 10.7%; OR=1.51; 95% CI: 1.29, 1.76; p<0.001).

Conclusions—LDL-C testing is recommended for patients with a history of ASCVD and may be a high-value and low-cost intervention to improve adherence and statin management.

Keywords

LDL-C testing; cardiovascular disease

Introduction

Patients who have had an atherosclerotic cardiovascular disease (ASCVD) event are at significant risk of another. Thus, aggressive secondary prevention is critical. However, inadequate patient adherence and failure to intensify treatment, when required, are significant challenges for prevention efforts.

ACC/AHA's 2013 Cholesterol Guideline[1] and the 2018 AHA/ACC Multi-society Cholesterol Guideline[2] recommended lipid testing after statin initiation as a Class I recommendation; the guidelines lacked specific low-density lipoprotein cholesterol (LDL-C) treatment targets, leading many to conclude that testing was not warranted.[3] Further, ACC/AHA's 2015 Focused Update of Secondary Prevention Lipid Performance Measures[4] and 2017 Clinical Performance and Quality Measures for Adults with ST-Elevation and Non-ST-Elevation Myocardial Infarction removed LDL-C testing as a quality metric.[5] The absence of recommendations for LDL-C targets after statin initiation and lack of testing as a quality metric have led to lower rates of LDL-C testing with unknown consequences for patient adherence or on providers' intensification of statin treatment when needed. This study sought to evaluate the association between outpatient LDL-C testing and subsequent statin adherence or intensification in patients after an atherosclerotic vascular disease (ASCVD) event. The study was approved by the Kaiser Permanente Northern California Institutional Review Board.

Methods

A longitudinal study was conducted to assess the association between having an LDL-C test after an ASCVD event and subsequent statin adherence or intensification. Participants were Kaiser Permanente Northern California adults (ages 18–90) hospitalized with an ASCVD event (myocardial infarction or stroke) during 01/01/2016 to 12/31/2017 with follow-up through 12/31/2019.

Outcomes were the prevalence of statin adherence and statin treatment intensification based on pharmacy dispensing data.[6,7] Secondary statin adherence was estimated using continuous medication gap (CMG), defined as the percentage of time that a patient lacks adequate pill supply, and was dichotomized as good (CMG≤20%) or inadequate (CMG>20%).[8,9] Statin intensification (yes/no) was determined for participants who were not already on high-intensity statins at baseline. Initiation of non-statins (ezetimibe, PCSK9i) were not counted as part of intensification definition.

The exposure of interest was the first outpatient LDL-C test during the 12 months after an ASCVD event; baseline for follow-up was the LDL-C test date. For the reference participants with no LDL-C test, incidence density sampling was used to assign a baseline date that matched the distribution of timing of LDL-C tests among those who had an LDL-C test. We excluded participants who did not maintain membership or pharmacy benefits during the year after their baseline.

Multivariate logistic regression models were specified to estimate the odds ratios (OR) for statin adherence and intensification among those with versus without LDL-C testing. Multivariable models were adjusted for age, sex, race/ethnicity, current smoking, hypertension, diabetes, body mass index and eGFR.

Results

There were 19,604 adults hospitalized with an ASCVD event (myocardial infarction or stroke); the mean age was 69.5 years and 33.0% were women (Table). The intensification analysis included 7,054 adults not already on high-intensity statins; the mean age was 71.0 years and 40.6% were women. Rates of good statin adherence were significantly higher (80.2% vs 75.9%; OR=1.38; 95% CI: 1,28, 1.49; p<0.001) among participants who had an LDL-C test (Figure). LDL-C testing was also associated with significantly higher rates of treatment intensification (16.1% vs 10.7%; OR=1.51; 95% CI: 1,29, 1.76; p<0.001).

Discussion

Adherence to lipid-lowering medications remains challenging, even after ASCVD events, and most patient-level interventions to improve adherence are costly and have limited effectiveness.[10] In this study of patients hospitalized for an ASCVD event, subsequent LDL-C testing was associated with significantly better adherence, despite the source population already exhibiting relatively good adherence.[11] Similarly, LDL-C testing was associated with significantly more statin intensification.

Responses to statin therapy can vary significantly between patients.[12] Without a follow-up LDL-C test in patients after an ASCVD event, it is challenging for the treating clinician to know whether the patient has achieved a treatment goal of ≥50% LDL-C reduction as recommended by the 2013 and the 2018 Cholesterol Guidelines or whether a patient already on high-intensity statins might benefit from the addition of non-statin therapies as recommended by the 2018 Cholesterol Guidelines.

Just as blood pressure and hemoglobin A1C are routinely checked in the management of patients with hypertension or diabetes, respectively, LDL-C testing is important in the management of cardiovascular disease risk. An order for LDL-C testing and the results can each be a basis for patient-provider discussions about adherence and treatment goals. Given the lack of effectiveness and high cost of patient-level adherence interventions, LDL-C test results may serve as a low-cost prompt to improve statin adherence for patients with inadequate adherence.[13] LDL-C testing in patients with ASCVD can reduce clinical inertia by prompting clinicians to take action in response to elevated LDL-C levels.[14] Restoring lipid measurement as a performance measure or quality metric after initiation of a lipid lowering therapy may provide useful feedback to providers and patients, especially in patients with ASCVD and would allow performance measures to align with clinical practice guidelines. Studies have already documented that clinicians are not measuring lipid panels in their patients as a result of misinterpretations of the ACC/AHA Cholesterol Guidelines.[15]

A limitation of this study is that the observational study design precludes establishing a causal relationship.

Conclusion

LDL-C testing in high-risk patients with prevalent ASCVD provides valuable information to patients and providers about the effectiveness of the current statin regimen at minimal cost and may improve adherence and intensification. Reinstatement of LDL-C testing as a performance measure or NCQA HEDIS quality measure for patients with prior ASCVD would align practice patterns for LDL-C testing with national guidelines.

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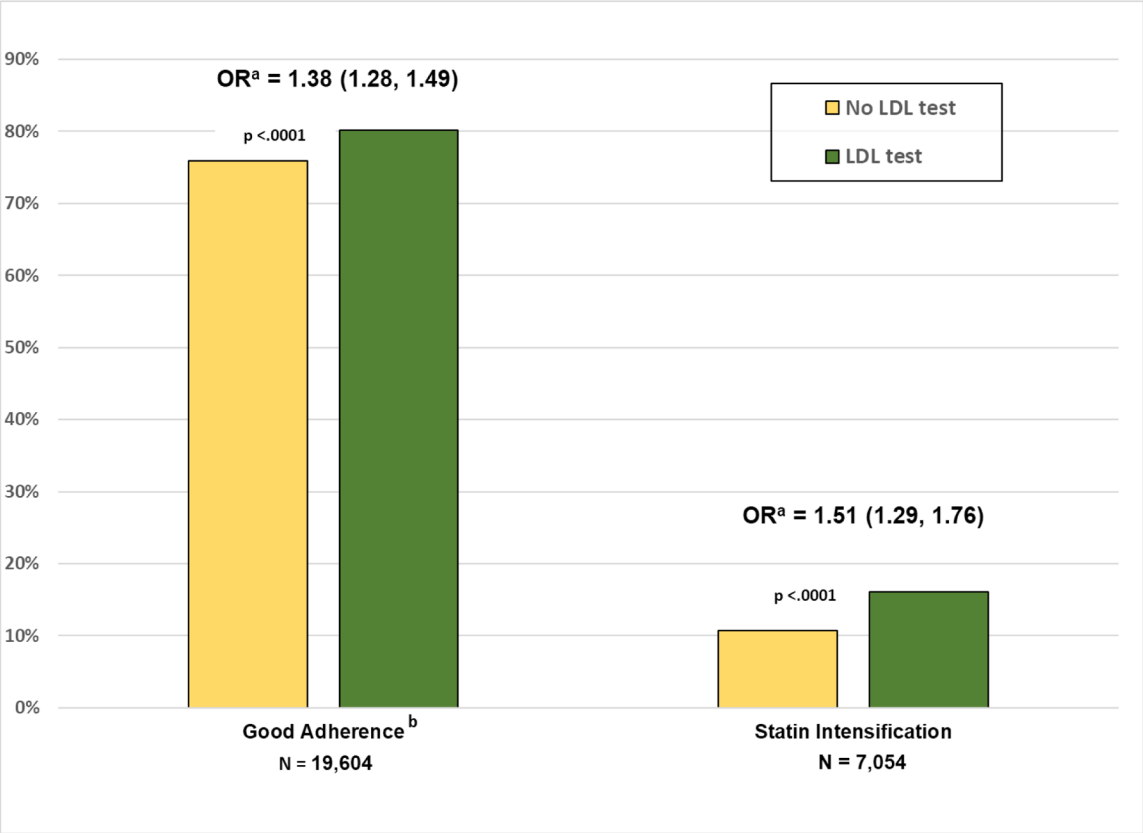

Figure:

Rates of statin adherence in the full sample and statin intensification among those not already on a high-intensity statin, with and without an LDL-C test after an ASCVD event.

[a]OR = odds ratios - adjusted for age, sex, race, current smoking, hypertension, diabetes, body mass index and GFR.

[b]Good Adherence = continuous medication gap (CMG) ≤ 20%.[8,9]

Table:

Characteristics at baseline (n=19,604)

	LDL-C test during follow-up		
	Yes (n=11,597)	**No (n=8,007)**	**χ^2 p - value**
Age, years (SD)	68.17 (11.3)	71.44 (11.8)	<.0001
Women	3,584 (30.9%)	2,943 (36.8%)	<.0001
Men	8,013 (69.1%)	5,064 (63.2%)	.
Race (self-reported)			
White	6,779 (58.5%)	4,984 (62.2%)	<.0001
Black	790 (6.8%)	703 (8.8%)	.
Latino	1,338 (11.5%)	854 (10.7%)	.
Asian	2,020 (17.4%)	1,012 (12.6%)	.
Other/Unknown	670 (5.8%)	454 (5.7%)	.
LDL-C, mg/dL (SD) - recorded within 2 years prior to baseline (N=13,711)	97.62 (40.5)	89.09 (37.2)	<.0001
Current smoker	628 (5.4%)	581 (7.3%)	<.0001
Hypertension	11,314 (97.6%)	7,720 (96.4%)	<.0001
Body mass index >30 kg/m^2	4,896 (42.3%)	3,272 (41.0%)	0.0601
Diabetes	4,955 (42.7%)	3,346 (41.8%)	0.1913
eGFR<60	3,231 (30.5%)	2,800 (38.3%)	<.0001
Adherence to statins			
Continuous medication gaps (CMG)[c]	0.12 (0.16)	0.14 (0.18)	<.0001
Adherent: 0%-20% CMG	9,301 (80.2%)	6,076 (75.9%)	<.0001
Non-adherent: > 20% CMG	2,296 (19.8%)	1,931 (24.1%)	.

[a] Hypertension definition?

[b] eGFR definition based on CKD-EPI Creatinine Equation

[c] CMG= continuous medication gaps; proportion of time with insufficient medication supply