Predictors of Statin Intolerance in Patients with a New Diagnosis of Atherosclerotic Cardiovascular Disease (ASCVD) Within a Large Integrated Healthcare Institution: THE IMPRES STUDY

TAMI L. BAIR[*] • HEIDI T. MAY[*] • KIRK U. KNOWLTON[*†] • JEFFREY L. ANDERSON[*†] • DONALD L. LAPPÉ[*] • JOSEPH B. MUHLESTEIN[*†]

[*] *Intermountain Medical Center Heart Institute, Salt Lake City, Utah, USA*

[†] *University of Utah, Salt Lake City, Utah, USA*

BACKGROUND

Statins are among the most prescribed medications due to the well-documented cardiovascular benefits of safely lowering LDL and they form an essential element of treatment strategy for patients with atherosclerotic cardiovascular disease.

However, many patients are unable or unwilling to continue statin therapy because of real or perceived adverse effects. Despite the established benefits of statin therapy, there is significant underuse in high-risk patients, with only around half continuing therapy.

Studies have shown that patients with statin intolerance are more likely to have adverse cardiovascular events and are more likely to undergo revascularization.

While some factors are known to increase the probability of statin intolerance, there is still much to learn about which patients are unlikely to tolerate statin therapy.

METHODS

The IMPRES Study evaluated ASCVD Intermountain Healthcare patients. Intermountain Healthcare is a nonprofit, integrated healthcare system including 22 hospitals, 185 clinics, and a system of health insurance plans.

All patients were included if they met the following criteria:

- Age ≥18 years of age
- Were documented to have ASCVD by one of the following:
  - Having a ***coronary artery*** related ASCVD event including:
    - Having a primary International Classification of Diseases, Ninth Revision, codes (ICD-9) inpatient diagnosis of coronary artery disease or acute myocardial infarction, or
    - Having undergone a documented percutaneous coronary intervention or coronary artery bypass graft surgery at Intermountain Healthcare.
  - Having a ***cerebrovascular*** related ASCVD event including:
    - Having a primary ICD-9 inpatient diagnosis of ischemic stroke, or
    - Having undergone a documented carotid artery endarterectomy or stenting at Intermountain Healthcare.
  - Having a ***peripheral arterial*** related ASCVD event including:
    - Having a primary ICD-9 inpatient diagnosis of peripheral arterial disease (PAD), or
    - Having undergone a documented aortic aneurysm repair or peripheral arterial revascularization procedure including bypass surgery or percutaneous intervention.

Inclusion criteria (continued):

- Survived their index encounter to hospital discharge
- Had an encounter documented in the Intermountain Healthcare electronic health record system between January 1, 1999 and December 31, 2013
- Had at least 3 years of follow-up data in the electronic health record system after the documented ASCVD diagnosis, or death within 3 years of index diagnosis, with a minimum of 2 encounters in the delivery system at least 12 months apart.

Statin intolerance was identified by ICD codes, clinician noted intolerance, and the use of pitavastatin which is primarily used when other statins are not tolerated.

Logistic regression was used to identify significant predictors of statin intolerance.

RESULTS

A total of 50,189 patients met inclusion criteria and were evaluated. Of those, 3,108 (6.2%) had a follow-up statin intolerance diagnosis. Of those with statin intolerance and having statin intensity information, 9.9% were prescribed a low, 73.3% moderate, and 16.8% high-intensity as their first statin dose received, respectively. Those first prescribed low (7.7% [275/3,551]) were more likely to be diagnosed with statin intolerance compared to moderate (5.9% [2,040/34,755]) or high (6.4% [467/7,246]).

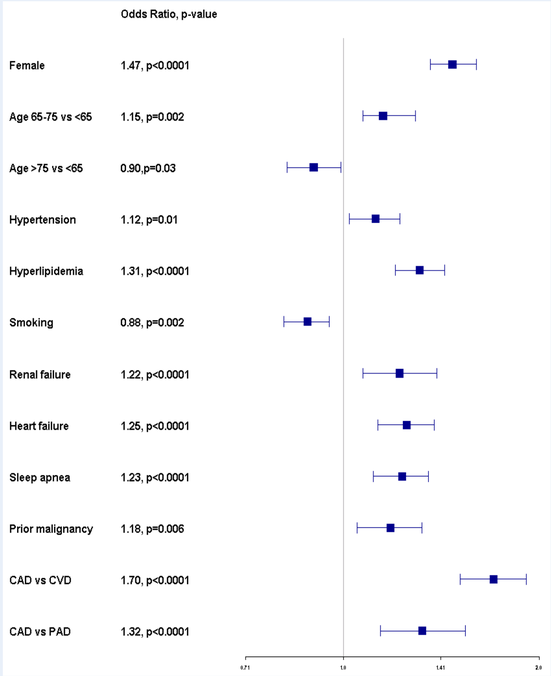
In a multivariable model, significant predictors of statin intolerance included female sex, younger age, hypertension, hyperlipidemia, non-smoking status, renal failure, heart failure, sleep apnea, prior malignancy, and index ASCVD diagnosis, but not depression, diabetes, atrial fibrillation, or COPD.

The median number of days from initial statin prescription after index ASCVD event to diagnosis of statin intolerance was 413.

TABLE 1: BASELINE CHARACTERISTICS

	No statin intolerance n=47,081	Statin intolerance n=3,108	p-value*
Sex (male)	32,242 (68.5%)	1,885 (60.6%)	<0.0001
Age			<0.0001
<65	20,739 (44.0%)	1,277 (41.1%)	
65-74	13,834 (29.4%)	1,045 (33.6%)	
>75	12,508 (26.6%)	786 (25.3%)	
Hypertension	32,793 (69.7%)	2,322 (74.7%)	<0.0001
Hyperlipidemia	30,773 (65.4%)	2,247 (72.3%)	<0.0001
Diabetes	13,952 (29.6%)	1,042 (33.5%)	<0.0001
ASCVD index diagnosis			<0.0001
CAD	36,332 (77.2%)	2,574 (82.8%)	
CVD	7,308 (15.5%)	342 (11.0%)	
PAD	3,441 (7.3%)	192 (6.2%)	
Smoking	17,021 (36.2%)	1,021 (32.9%)	0.06
Renal failure	3,171 (6.7%)	283 (9.1%)	<0.0001
History of depression	4,915 (10.4%)	403 (13.0%)	<0.0001
Heart failure	7,194 (15.3%)	624 (20.1%)	<0.0001
Atrial fibrillation	7,593 (16.1%)	572 (18.4%)	0.001
COPD	4,308 (9.2%)	301 (9.7%)	0.32
Sleep apnea	6,500 (13.8%)	530 (17.1%)	<0.0001
Prior malignancy	4,716 (10.0%)	367 (11.8%)	0.001
BMI category (kg/m^2)			0.19
<25	10,432 (23.2%)	663 (22.3%)	
25-29.9	17,301 (38.4%)	1,117 (37.6%)	
≥30	17,274 (38.4%)	1,189 (40.0%)	

FIGURE 1: MULTIVARIATE PREDICTORS OF STATIN INTOLERANCE DIAGNOSIS



CONCLUSIONS

Female sex and many standard cardiovascular risk factors were associated with statin intolerance, suggesting that patients with more comorbidities are likely to have statin intolerance. However, additional study is needed to determine if statin intolerance may also be predicted by other non-measured variables, such as genetic polymorphisms and psychosocial factors.

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