**Genetic Testing for Statin-Induced Myopathy**

**Effective:** April 1, 2020

**Next Review:** January 2021  
**Last Review:** February 2020

**IMPORTANT REMINDER**

Medical Policies are developed to provide guidance for members and providers regarding coverage in accordance with contract terms. Benefit determinations are based in all cases on the applicable contract language. To the extent there may be any conflict between the Medical Policy and contract language, the contract language takes precedence.

PLEASE NOTE: Contracts exclude from coverage, among other things, services or procedures that are considered investigational or cosmetic. Providers may bill members for services or procedures that are considered investigational or cosmetic. Providers are encouraged to inform members before rendering such services that the members are likely to be financially responsible for the cost of these services.

**DESCRIPTION**

HMG-CoA reductase inhibitors, or statins, which are widely used to treat hypercholesterolemia, can cause muscle-related adverse events. Serious myopathy (i.e., myositis, rhabdomyolysis) can also occur and may be associated with variants in the *SLCO1B1* gene.

**MEDICAL POLICY CRITERIA**

Genetic testing for the presence of variants in the *SLCO1B1* gene to identify patients at risk of statin-induced myopathy is considered **not medically necessary**.

**NOTE:** A summary of the supporting rationale for the policy criteria is at the end of the policy.

**CROSS REFERENCES**

None

**BACKGROUND**

HMG-CoA reductase inhibitors, or statin drugs, are the primary pharmacologic treatment for hypercholesterolemia worldwide. In the United States, an estimated 38 million people took statins in 2008.[1] The use of statins is associated with an approximately 30% reduction in
cardiovascular events across a wide variety of populations.[2]

STATIN-INDUCED MYOPATHY

Statins are associated with a known risk of muscle-related symptoms, which are the most common adverse effects of statin drugs. Myopathy is a general term for muscle toxicity. Three categories of statin-induced myopathy were defined in 2002 by a joint committee of the American College of Cardiology, American Heart Association, and National Heart, Lung and Blood Institute[3]:

- Statin-induced myalgia, defined as any muscle symptoms that occur without an elevation of serum creatinine kinase;
- Statin-induced myositis, defined as muscle symptoms with an elevation of serum creatinine kinase; and
- Statin-induced rhabdomyolysis, defined as markedly severe muscle symptoms with an elevation of creatinine kinase greater than 10 times normal with an elevation in serum creatinine.

Statin-induced myalgia is the most common manifestation of myopathy; it is characterized by muscle pain, cramps, fatigue, and/or weakness.[4] Myalgias without other clinical manifestations are not associated with clinically important adverse events and resolve when the statin is discontinued.

The incidence of myalgia varies widely. In clinical trials, these have been reported in 1.5% to 3.0% of patients; in most trials, the rate of myalgias in patients on statin therapy is not increased compared with placebo treatment.[5] In observational studies, higher rates of 10% to 15% have been reported.[2]

Myositis is much less common than myalgias, with an estimated rate of 5 per 100,000 patient-years, and an estimated per-person incidence of 0.01%.[5] In virtually all cases, myositis resolves with discontinuation of the statin.

Rhabdomyolysis is the most severe clinical manifestation of statin-induced myopathy and can be life-threatening. The National Lipid Association estimated that rhabdomyolysis occurs at a rate of 1.6 per 100,000 patient-years, and the U.S. Food and Drug Administration (FDA) adverse events reporting system has estimated a rate of 0.7 per 100,000 patient-years.[5] A 2006 systematic review combined results from 20 clinical trials and estimated the rate of rhabdomyolysis to be 1.6 cases per 100,000 patient-years.[6] Fatalities from statin-induced rhabdomyolysis can occur, but the mortality rate is not well-defined. FDA estimated that deaths from rhabdomyolysis occur at a rate of less than 1 death per million prescriptions.[3]

A number of clinical factors are associated with an increased risk of statin myopathy. Statin dose is probably the strongest risk factor, with an estimated 6-fold increase for patients on high-dose statins[7] (age is also a strong risk factor). One 2007 study reported that patients older than 65 years of age required hospitalization for statin-induced myositis at a rate that was 4 times higher than for younger patients.[8] Some statins may be associated with higher risk than others, and concomitant administration of certain drugs (eg, gemfibrozil, amiodarone) has been associated with higher rates of statin myopathy in clinical trials.[7] Other factors that may be associated with myopathy include female sex and intense physical exercise.[7] The perceived risk of statin-induced myopathy may contribute to suboptimal statin use in patients...
with indications. It is estimated that less than 50% of patients in the United States who would benefit from statins are currently taking them, a substantial percentage of whom do not adhere to prescribed statin regimens.[1]

GENETIC FACTORS ASSOCIATED WITH STATIN-INDUCED MYOPATHY

A variety of genetic factors are associated with statin myopathy. The cytochrome p450 system in the liver is the main pathway by which statins are metabolized. Numerous genetic variants in cytochrome p450 proteins affect the pharmacokinetics of statin metabolism and serum statin levels.[2] Other genetic variants affect statin metabolism, efficacy, and susceptibility to adverse effects; these genetic variants involve variations in the apolipoproteins such as apo E, variations in the cholesterol ester transfer proteins, or variations in the coenzyme Q pathway.[1]

Variations in the SLCO1B1 gene also affect statin metabolism and are among the most well studied genetic variants. These variants are the genetic markers for which there are commercially available tests. This gene codes for a transporter protein that is part of the solute carrier organic ion transporter system, which mediates the influx and metabolism of statins in the liver.[2] Single nucleotide variants (SNVs) in this gene are associated with variations in the risk of statin-induced myopathy. The T/T allele is the wild-type and associated with the lowest risk of myopathy. The C/C allele is associated with the highest risk of myopathy, and the T/C allele with an intermediate risk. The T allele has a prevalence of approximately 0.87, and the C allele has a prevalence of approximately 0.13.[4]

Other genes have also been studied, including ABCB1, which encodes ATP-binding cassette (ABC) transporters subfamily B member 1 (ABCB1/P-glycoprotein 1), ABCG2, which encodes ABC transporters subfamily G member 2 (ABCG2/breast cancer resistance protein), and the coenzyme Q2 (COQ2) homolog gene. Other studies have evaluated the association between variants in the GATM gene and statin-induced myopathy (the GATM gene encodes a glycine amidinotransferase that is the rate-limited enzyme in creatine biosynthesis). However, it should be noted that the association between variants has not been consistently replicated.[9]

Commercially Available SLCO1B Molecular Diagnostic Tests

Several commercial and academic labs offer genetic testing for statin-induced myopathy (SLCO1B1) variants. For example, Boston Heart Diagnostics markets a test for the (SLCO1B1) genotype. This test uses real-time polymerase chain reaction to identify patients with the T/T, T/C, or C/C genotype.[10]

ARUP Laboratories (Salt Lake City, UT) markets a test for SLCO1B1 variants that uses real-time polymerase chain reaction with high-resolution melting analysis to identify the rs4149056C variant in the SLCO1B1 gene.[11]

Some labs offer panel tests for drug metabolism, which may use Sanger sequencing or next-generation sequencing, that include the SLCO1B1 gene; for example, ApolloGen (Irvine, CA) markets a pharmacogenomics panel, the iGene Pharmacogenomics Panel, that sequences the SLCO1B1 gene.[12]

REGULATORY STATUS

Clinical laboratories may develop and validate tests in-house and market them as a laboratory service; laboratory-developed tests must meet the general regulatory standards of the Clinical Laboratory Improvement Amendments. The Boston Heart Statin Induced Myopathy
(SLCO1B1) Genotype test and ARUP Laboratories Statin Sensitivity SLCO1B1 are available under the auspices of the Clinical Laboratory Improvement Amendments. Laboratories that offer laboratory-developed tests must be licensed by the Clinical Laboratory Improvement Amendments for high-complexity testing. To date, FDA has chosen not to require any regulatory review of this test.

**EVIDENCE SUMMARY**

Human Genome Variation Society (HGVS) nomenclature[13] is used to describe variants found in DNA and serves as an international standard. It is being implemented for genetic testing medical evidence review updates starting in 2017. According to this nomenclature, the term “variant” is used to describe a change in a DNA or protein sequence, replacing previously-used terms, such as “mutation.” Pathogenic variants are variants associated with disease, while benign variants are not. The majority of genetic changes have unknown effects on human health, and these are referred to as variants of uncertain significance.

Validation of the clinical use of any genetic test focuses on 3 main principles: (1) analytic validity, which refers to the technical accuracy of the test in detecting a variant that is present or excluding a variant that is absent; (2) clinical validity, which refers to the diagnostic performance of the test (sensitivity, specificity, positive and negative predictive values) in detecting clinical disease; and (3) clinical utility (ie, how the results of the diagnostic test will be used to change management of the patient, and whether these changes in management lead to clinically important improvements in health outcomes). The following is a summary of the key literature.

**TESTING FOR SLCO1B1 VARIANTS**

**Clinical Context and Test Purpose**

The purpose of genetic testing for SLCO1B1 variants in patients who are taking statin drugs is to inform a decision whether patients identified as at risk for statin-associated myopathy should continue taking statin drugs.

**Analytic Validity**

At least 2 labs (Boston Heart Diagnostics, ARUP Laboratories) perform the statin-induced myopathy test using real-time polymerase chain reaction. This technique permits detection and amplification of DNA fragments simultaneously. While an accepted method of genetic analysis with generally high accuracy, no published information was found on the accuracy of this technique for detecting genetic variants associated with statin-induced myopathy. ARUP Laboratories has reported that the test’s analytic sensitivity and specificity are greater than 99% for identification of the presence of 1 or 2 copies of SLCO1B1*5.[14]

**Clinical Validity**

No studies were identified that reported the sensitivity or specificity of genetic testing for statin-induced myopathy in populations with suspected statin-induced myopathy. Studies that were identified have reported the degree of risk for myopathy associated with the SLCO1B1 genetic variants. Those studies include genome-wide association studies, case-control studies, cohort analyses, and clinical trials. Representative types of each study are discussed next.

**Randomized Controlled Trials**
Genome-wide association studies have reported that \textit{SLCO1B1} variants are associated with statin-induced myopathy. The SEARCH study group published a genome-wide association study in 2008 based on data from a randomized controlled trial of 12,064 patients with a prior myocardial infarction assigned to simvastatin 80 mg or simvastatin 20 mg. Of the 6031 patients in the 80-mg statin group, 48 (0.8%) had elevated serum creatinine kinase (CK) level more than 10 times normal, and an additional 48 (0.8%) patients had a CK level that was more than 3 times normal and more than 5 times the baseline level. These subjects were matched with 96 control subjects without CK elevation, matched for sex, age, renal function, and ancillary medication use. Adequate DNA samples were available for 85 patients with myopathy and 90 controls, and these patients formed the study group for derivation of the genome associations.

The \textit{SLCO1B1} locus was the single nucleotide variants that had a strong association with myopathy, at a corrected p value of 0.001. The estimated odds ratio (OR) for myopathy in patients with a single C allele was 4.3 (95% confidence interval [CI], 2.5 to 7.2), and the estimated odds for patients homozygous for the C allele was 17.4 (95% CI, 4.8 to 62.9). Based on these data, the cumulative risk of developing myopathy after 6 years of treatment with simvastatin 80 mg was 0.6% for patients with the T/T allele, 3% for patients with the T/C allele, and 18% for patients with the C/C allele. Other clinical factors that predicted a risk of myopathy were female sex (relative risk [RR], 1.8; 95% CI, 1.1 to 2.8), age 65 and older (RR=2.2; 95% CI, 1.4 to 3.4), impaired renal function (RR=2.2; 95% CI, 1.4 to 3.4), use of amiodarone (RR=6.4; 95% CI, 3.4 to 12.1), use of calcium antagonists (RR=1.7; 95% CI, 1.2 to 2.6), and diabetes (RR=1.7; 95% CI, 1.0 to 2.9).

SEARCH investigators replicated the association of the \textit{SLCO1B1} genetic variant with myopathy in 16,664 patients from a separate randomized controlled trial, the Heart Protection Study. In this study, all patients were treated with simvastatin 40 mg, and 23 (0.1%) were identified with CK levels greater than 10 times normal. \textit{SLCO1B1} variants were also strongly associated with myopathy in this replication study, with a corrected p value of 0.004. The estimated odds ratio for the presence of a C allele was 2.6 (95% CI, 1.3 to 5.0).

The STRENGTH (Statin Response Examined by Genetic Haplotype Markers) study was a randomized trial that examined statin response and safety by dose of statin, statin type, and presence of genetic markers. A total of 509 patients were randomized to various doses of atorvastatin, pravastatin, or simvastatin and followed for adverse events, including myopathy. The presence of at least 1 variant on the \textit{SLCO1B1} gene was associated with an increased rate of adverse events (37% vs 25%, p=0.03). There was also evidence of a “dose-response” effect, with the risk of adverse events being 19% with no variant alleles, 27% with 1 variant allele, and 50% with 2 variant alleles (p=0.01 for trend). The association between \textit{SLCO1B1} gene status and adverse event rates did not appear to be present for patients who received pravastatin.

Case-Control and Cohort Studies

A case-control study reporting on the risk of myopathy associated with \textit{SLCO1B1} variants was reported in 2012. This study by Brunham identified cases with statin-induced myopathy, defined as muscle symptoms with a CK elevation at least 10 times normal, from 2 large lipid clinics in the Netherlands. Twenty-five cases of myopathy were identified from 9000 total patients, for a prevalence of 0.26%. These patients were matched for age, sex, statin type, and statin dose, with 84 patients who did not have myopathy. In the whole cohort of patients taking
any statin, there was a nonsignificant trend toward an increase in myopathy for patients with a
SLCO1B1 variant (OR=1.5; 95% CI, 0.58 to 3.69; p=0.21). When restricted to patients on
simvastatin, the association was stronger but not statistically significant (OR=3.2; 95% CI, 0.83
to 11.96; p=0.06).

Carr (2013) reported results from a similar case-control study evaluating the risk of statin-
induced myopathy associated with SLCO1B1 variants.[17] The authors identified 77 statin-
induced myopathy patients (serum CK >4 times the upper limit of normal) and 372 statin-
tolerant controls from a U.K. large database of anonymous longitudinal medical records. In
multiple logistic regression analyses to determine statin-associated myopathy risk, the
presence of the C allele in the SLCO1B1 gene was significantly associated with myopathy: for
all myopathy, the adjusted odds per C allele was 2.08 (95% CI, 1.3 to 3.32); for severe
myopathy, the adjusted odds per C allele was 4.47 (95% CI, 1.84 to 10.84). When analysis
was restricted to only those patients receiving simvastatin (n=281), there was a significant
association between the SLCO1B1 gene status and myopathy (adjusted OR per C allele, 2.13;
95% CI, 1.29 to 3.54; p=0.014). In contrast, when the analysis was restricted to only those
patients receiving atorvastatin (n=121), no significant association was found. Variations in the
COQ2 gene were not associated with statin-induced myopathy.

Some evidence, including the Carr results, has suggested that the association between
myopathy and SLCO1B1 genotype is most pronounced for simvastatin. Danik (2013)
evaluated the role of SLCO1B1 variants as effect modifiers for clinical myalgia in the
Prevention: an Intervention Trial Evaluating Rosuvastatin (JUPITER) trial, which randomized
subjects to rosuvastatin (20 mg/d) or placebo.[18] Among the 4404 subjects allocated to
rosuvastatin, there was no significant association between SLCO1B1 gene status and either
muscle symptoms or a diagnosis of rhabdomyolysis, myopathy, or myositis.

In a subanalysis of a prospective population-based cohort study of chronic diseases in the
elderly population, de Keyser (2014) evaluated whether SLCO1B1 variants modify the risk of
adverse drug reactions during statin therapy among 2080 patients who received simvastatin or
atorvastatin and had SLCO1B1 genotype available.[19] The study’s primary outcome was a
reduction in statin dose or a switch to another statin-lowering drug as an indicator for an
adverse drug reaction. Among simvastatin users, the T>C variant was significantly associated
with the primary outcome. Patients with the CC genotype had a hazard ratio for dose decrease
or switch of 1.74 (95% CI, 1.05 to 2.88). A similar association was not seen among atorvastatin
users.

Ferrari (2014) conducted a case-control study among patients treated with atorvastatin,
rosuvastatin, or simvastatin to assess the contribution of variants in the SLCO1B1, ABCB1,
and ABCG2 genes to the risk of statin-induced myopathy.[20] Cases (n=33) included patients
with statin-induced elevations in serum CK levels of greater than 3 times the upper limit of
normal; they were compared with 33 matched controls. Patients with increased CK levels had
significantly increased odds for the SLCO1B1 C allele (OR=8.86; p<0.01) or the ABCB1 T
allele (OR=4.67; p<0.05). Patients with increased CK levels did not have significantly
increased odds of having the ABCG2 genotype.

Canestaro (2014) conducted a systematic review of studies evaluating the association
between a number of genetic variants, including SLCO1B1, and statin serum concentrations
and subsequent myopathy.[21] Thirteen studies were identified, which evaluated 7 genes in
classes: 3 cytochrome p450 enzymes (CYP2D6, CYP3A4, CYP3A5), the mitochondrial
enzyme glycine amidinotransferase (GATM), SLCO1B1, and the cell efflux transporters genes (ABCB1, ABCG2). The STRENGTH and SEARCH studies, along with the 2012 Brunham study, were included in the systematic review. Reviewers concluded that the evidence for an association between the *5 allele of the SLCO1B1 gene and statin-related myopathy was strong and replicated in multiple studies, particularly for simvastatin. A 2015 meta-analysis of case-control studies supported these findings; the variant C allele, in particular, increased the risk of severe myopathy. The increased risk was observed for simvastatin but not atorvastatin.

A small cohort study (N=26) published by Elam (2017) analyzed 16 patients with a history of discontinuation of one or more statins due to statin myalgia without significant elevation in creatine phosphokinase (>5-fold above normal) compared with a statin-tolerant control (n=10). Age ranged from 46 to 78 years (mean, 65.4 years in the re-challenge group; mean, 60.9 years in the control group), and the groups were parallel in terms of disease history and laboratory characteristics, except for statistically significant differences in: use of vitamin D supplements (p=0.04) and testosterone (p=0.01); and variation in levels of high-sensitivity C-reactive protein (CRP; p=0.002), cholesterol (p=0.002), and low-density lipoprotein cholesterol (p=0.008). In addition to the reporting of muscle symptoms, the analysis consisted of subjecting differentially expressed genes to Ingenuity Pathway Analysis and DAVID (Database for Annotation, Visualization and Integrated Discovery) to establish the presence of disruption in gene expression and metabolic pathways in skeletal muscles.

Most cases (75%) had a recurrence of muscle symptoms during the re-challenge; and nearly one-third (31%) on average discontinued statin treatment within 9.3 days (range, 3-14 days) due to symptoms. The most prominent pathways altered by statins included:

- **TP53** (response to cellular stress)
- **BARD1, MR11, RAD51** (tumor suppression, apoptosis, cell senescence, DNA repair)
- **CXCL12, CST5, POU2F1** (activation of proinflammatory immune response)
- **FDFT1, LSS, TP53, UBD, ATF2, H-ras** (protein catabolism, cholesterol biosynthesis, protein prenylation, RAS-GTPase activation).

These pathway alterations suggest that cellular stress and inflammatory immune responses may contribute to the development of statin-related myalgia. Three single nucleotide variants associated presented with increased frequency among patients with statin myalgia (SLCO1B1, p=0.039; SLC02B1, p=0.01; RYR2, p=0.16). The authors of the cohort study suggested that an increase in the expression of mevalonate pathway enzymes downstream of HMG-CoA reductase in patients with statin-induced myalgia reflects a genetic predisposition to myopathies via increased exposure of muscle to statin. However, they concluded that these findings are tentative and must be validated, noting several limitations. Single gene associations are representative only and did not pass genome-wide test correction thresholds. The gene networks identified in pathway analyses represent statistical associations rather than causality. The analyses did not exclude changes in miRNA, protein expression or activity, or epigenetic changes. Intolerance to statins can occur even after periods of tolerance.

In contrast to the positive associations found among single nucleotide variants with statin-related myopathies in other studies, a small retrospective analysis (N=52) in Japan by Sai (2016) did not find statistically significant associations for SLCO1B1 or GATM. However, the
analysis did find an association for HLA-DRB1 (OR=3.19; p=0.003) that was significant, suggesting a possible association with the onset of statin-related myopathies. The authors noted that while the findings were suggestive of possible ethnic-related genetic markers, the study required further validation and variation in dosage and type of statin used in Japan compared with the U.S. limits generalizability.

A prospective analysis by Stranecky (2016) assessed the genomic data for 86 patients (age range, 29-84 years) in Prague who were being treated with statins for hypercholesterolemia and suffering from statin-related myopathy. The authors used whole genome genotyping to investigate the possible contribution of large copy-number variants (CNVs) in the development of symptoms. Patients (65% women) received either simvastatin, atorvastatin, rosuvastatin, or combination throughout a 4-year period. There were 53 (62%) cases of myopathy and 34 (40%) cases of muscle symptoms reported. No large CNVs were found in the \textit{SLCO1B} region; moreover, there were no large CNVs associated with statin-related myopathy. The authors reported no limitations to the study.

**Section Summary: Clinical Validity**

The available evidence from genome-wide association studies has suggested that \textit{SLCO1B1} variants are associated with the risk of statin-associated myopathy. Prospective case-control studies and randomized controlled trials have been mixed in demonstrating an association between \textit{SLCO1B1} variants and statin-associated myopathy. A small Japanese study requiring further validation found a possible association to ethnic-related genetic markers. Additionally, large CNVs with the potential to affect genes involved in drug metabolism and muscle function have not been found to play a role in the etiology of statin-related myopathy.

**Clinical Utility**

No studies identified reported direct evidence on the clinical utility of genetic testing for statin myopathy. Direct evidence for clinical utility in this setting would come from studies demonstrating that using the \textit{SLCO1B1} genotype to inform statin therapy (statin dose or choice of specific drug) has positive outcomes in terms of lower rates of myopathy with adequate lipid control and tolerability of alternative treatments. Indirect evidence includes the predicted number of patients who avoid statin myopathy as a result of genetic testing. This number is uncertain because there are a number of actions that can be taken as a result of genetic testing. Statins can be stopped or not started, a lower dose can be used, and other risk factors can be avoided, such as use of amiodarone. Despite the uncertainty in the precise number of events avoided, the number will necessarily be low because of the low underlying rate of serious events.

Vassy (2018) conducted a systematic review of \textit{SLCO1B1} testing on patient and healthcare outcomes. They identified 5 pilot studies and an RCT by Voora (2017) that studied the delivery of \textit{SLCO1B1} results on patient outcomes. Voora recruited patients who had discontinued statin therapy due to suspected side effects (73% reported myalgia and 25% of patients were \textit{SLCO1B1*5} carriers). Patients were randomized to either immediate or delayed results of \textit{SLCO1B1} testing, stratified based on \textit{SLCO1B1*5} genotype (carriers vs noncarriers) and clinic site. The primary outcome was adherence as assessed by the Morisky Medication Adherence Scale. Secondary outcomes included low density lipoprotein (LDL) cholesterol, brief pain inventory and SF-12. Voora reported a significant difference between groups in LDL at 3 months, but not in other outcome measures.
Several institutions have implemented electronic medical record–based clinical decision support systems to guide statin dosing and follow-up for patients started on a statin using a patients’ SLCO1B1 status.[7,27] However, it should be noted that all studies seeking to demonstrate that such support systems are associated with improved clinical outcomes have been found to be lacking.

When statin use is reduced or eliminated, the reduction in statin myopathy needs to be weighed against the increased cardiovascular events that may occur as a result of this change. In patients with a moderate-to-high risk of cardiovascular events, the probability of myocardial infarction over a 10-year period may be in the range of 10% to 20%. This event rate is substantially higher than the probability of serious myositis and rhabdomyolysis. As a result, if statin drugs are avoided because of genetic testing, the number of myocardial infarctions that will result may exceed the number of myopathy episodes avoided, and net harm may result. Because there are no alternative agents that reduce the rate of cardiovascular events to the extent statins do, it may not be possible to ameliorate this net harm by changing to an alternative lipid-lowering strategy.

Section Summary: Clinical Utility

The available evidence is insufficient to demonstrate that the clinical use of SLCO1B1 genotyping is associated with subsequent changes in patient management and/or improved outcomes, or with increased adherence to statin therapy.

Summary of Evidence

For individuals who are taking statin drugs who receive genetic testing for SLCO1B1 variants, the evidence includes secondary analyses of randomized controlled trials and prospective observational studies. Relevant outcomes are test accuracy and validity, morbid events, and hospitalizations. No published information was found on the analytic validity of the marketed tests for detecting genetic variants associated with statin-induced myopathy. The available evidence from genome-wide association studies has suggested that SLCO1B1 variants are associated with risk of statin-associated myopathy. Observational studies and randomized controlled trials have been mixed in demonstrating an association between SLCO1B1 variants and statin-associated myopathy. No studies identified reported direct evidence on the clinical utility of genetic testing for statin myopathy. Statins are associated with a definitive decreased risk of cardiovascular events such as myocardial infarction, and this benefit of reduced cardiovascular events is likely to far outweigh the risk of myopathy—even in individuals with the highest risk of myopathy (ie, those with two abnormal SLCO1B1 alleles). Therefore, there is a possibility of harm if the results of a positive test for statin-induced myopathy are used as part of the decision-making process for prescribing statins. The evidence is insufficient to determine the effects of the technology on health outcomes.

PRACTICE GUIDELINE SUMMARY

In 2012, the Clinical Pharmacogenetics and Pharmacogenomics Implementation Consortium issued guidelines for SLCO1B genotypes and simvastatin-induced myopathy, which were updated in 2014.[28] These guidelines on patient management for various SLCO1B genotypes recommended prescribing a lower dose or considering an alternative statin and considering routine creatinine kinase surveillance in patients with SLCO1B genotypes consistent with intermediate or low statin metabolism.
SUMMARY

HMG-CoA reductase inhibitors, or statins, which are widely used to treat hypercholesterolemia, can cause muscle-related adverse events. Serious myopathy (ie, myositis, rhabdomyolysis) can also occur and may be associated with variants in the SLCO1B1 gene. Commercially available tests for the presence of SLCO1B1 variants are marketed for use in predicting the risk of myopathy for patients taking statins.

There is not enough evidence to show that genetic testing for SLCO1B1 is effective in identifying patients at-risk for statin-induced myopathy. No clinical guidelines based on research recommend the use of SLCO1B1 genetic testing for identifying patients at-risk for statin-induced myopathy. Therefore, genetic testing for SLCO1B1 variants to identify patients at-risk for statin-induced myopathy is considered not medically necessary.

REFERENCES


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