Can Statins Cut the Benefits of Exercise?

By GRETCHEN REYNOLDS

An important new study suggests that statins, the cholesterol-lowering medications that are the most prescribed drugs in the world, may block some of the fitness benefits of exercise, one of the surest ways to improve health.

No one is saying that people with high cholesterol or a family history of heart disease should avoid statins, which studies show can be lifesaving. But the discovery could create something of a dilemma for doctors and patients, since the people who should benefit the most from exercise — those who are sedentary, overweight, at risk of heart disease or middle-aged — are also the people most likely to be put on statins, possibly undoing some of the good of their workouts.

For the new study, which was published online in The Journal of the American College of Cardiology, researchers from the University of Missouri and other institutions gathered a group of overweight, sedentary men and women, all of whom had multiple symptoms of metabolic problems, including wide waistlines, high blood pressure or excess abdominal fat.

Most had slightly but not dangerously elevated cholesterol levels.

None had exercised regularly in the past year.

All underwent muscle biopsies and treadmill testing to determine their aerobic fitness — which was generally quite low — and agreed to continue with their normal diet.

Then they all began a supervised 12-week exercise program, during which they visited the university lab five times a week and walked or jogged on a treadmill for 45 minutes at a moderately vigorous pace (about 65 to 70 percent of their individual aerobic maximum).

Half of the group also began taking a daily 40-milligram dose of simvastatin, a particular type of statin sold under the brand name Zocor.

At the end of 12 weeks, the participants fitness and muscles were retested.

Statins, as most of us know, are medications designed to reduce the body’s cholesterol levels, particularly levels of low-density lipoprotein, or “bad” cholesterol. The drugs routinely are prescribed for those with high cholesterol and other risk factors for heart disease, and some physicians believe that they should be used prophylactically by virtually everyone over 50.
Exercise also typically is recommended as a means of fighting heart disease and prolonging life span.

And both statins and sweating indisputably are effective. In past studies, researchers have shown that statins reduce the risk of a heart attack in people at high risk by 10 to 20 percent for every 1-millimole-per-liter reduction in blood cholesterol levels (millimoles measure the actual number of cholesterol molecules in the bloodstream), equivalent to about a 40-point drop in LDL levels. Meanwhile, improving aerobic fitness by even a small percentage through exercise likewise has been found to lessen someone’s likelihood of dying prematurely by as much as 50 percent.

So, theoretically, it would seem that combining statins and exercise should provide the greatest possible health benefit.

But until the current study, no experiment scrupulously had explored the interactions of statin drugs and workouts in people. And the results, as it turns out, are worrisome.

The unmedicated volunteers improved their aerobic fitness significantly after three months of exercise, by more than 10 percent on average. But the volunteers taking the statins gained barely 1 percent on average in their fitness, and some possessed less aerobic capacity at the end of the study than at its start.

Why there should be such a discrepancy between the two groups’ fitness levels wasn’t clear on the surface. But when the researchers looked microscopically at biopsied muscle tissue, they found notable differences in the levels of an enzyme related to the health of mitochondria, the tiny energy-producing parts of a cell. Mitochondria generally increase in number and potency when someone exercises.

But in the volunteers taking statins, enzyme levels related to mitochondrial health fell by about 4.5 percent over the course of the experiment. The same levels increased by 13 percent in the group not taking the drug.

In effect, the volunteers taking statins “were not getting the same bang from their exercise buck” as the other exercisers, says John P. Thyfault, a professor of nutrition and exercise physiology at the University of Missouri and senior author of the study.

This finding joins a small but accumulating body of other studies indicating that statins can negatively affect exercise response. Lab rodents given statins, for instance, can’t run as far as unmedicated animals, while in humans, marathon runners on statins develop more markers of muscle damage after a race than runners not using the drugs.

None of which suggests, Dr. Thyfault says, that statins are not worthwhile. For people who have a family history of high cholesterol or heart disease or who themselves have high cholesterol, he says, “there’s no doubt that statins save lives.”

But for other people, the risk-benefit calculation involving statins may be trickier in light of this and other new science.
“Low aerobic fitness is one of the best predictors” of premature death, Dr. Thyfault says. And if statins prevent people from raising their fitness through exercise, then “that is a concern.”

A possible remedy, he continues, could be for people to get in shape and raise their aerobic fitness before starting the drug, but that’s an issue to discuss with your doctor. “There’s still a great deal we don’t understand” about how statins and exercise mix, he says.
Small Study Suggests Statins May Blunt Benefits Of Exercise

A small study is raising big questions about whether statins may blunt the beneficial effects of exercise. The study has been published online in the Journal of the American College of Cardiology and was the subject of a New York Times blog today.

37 previously sedentary overweight or obese adults with at least 2 other risk factors underwent 12 weeks of aerobic exercising training. 19 patients were randomized to also receive a statin (simvastatin 40 mg/day). At the end of the study cardiorespiratory fitness, as measured by maximal oxygen uptake, had increased significantly by 10% in the control group but only by 1.5% in the simvastatin group. The control group also had a significant 13% increase in skeletal muscle citrate synthase activity, a measure of mitochondrial activity in muscles, compared with a 4.5% decrease in the simvastatin group. The authors, led by John Thyfault at the University of Missouri, said their results “suggest that simvastatin may mitigate improvements in fitness in response to exercise training by impairing increases in skeletal muscle mitochondrial content and function.”

The authors concluded: “Given the strong independent cardio-protective effects of increasing cardiorespiratory fitness or lowering LDL, the benefits and risks of each should be carefully considered when choosing treatment modalities.”

The study raises troubling questions about the interactions of statins and exercise, but its small size, along with other limitations, may limit its immediate impact. In an accompanying editorial, Paul Thompson and Beth Parker take note of several of these limitations. For one, because the control group did not take a placebo pill, participants were not blinded to their treatment. They cite evidence that people on statins are likely to overestimate the skeletal muscle side effects of statins.

They also note that the researchers did not report whether the two groups achieved similar levels of exercise intensity:

We have observed a reduction in spontaneous physical activity levels in individuals over age 55 years treated with atorvastatin. Knowing whether or not the statin-treated subjects exercise-trained less intensely... would indicate if statins reduced the training stimulus itself or if they reduced the physiological response to a similar training stimulus.
Thompson and Parker also cite a recent analysis published in the *Lancet* that found that both statins and increased physical fitness were independently associated with low mortality but that “the combination of statin treatment and increased fitness resulted in substantially lower mortality risk than either alone.” This suggests that the short-term changes in surrogate endpoints seen in the *JACC* study, even if found to be true, may not result in important long-term differences in health.

Robert Eckel, speaking on behalf of the American Heart Association, raised several other questions about the study. “The bottom line,” he said, is that the simvastatin 40 mg regimen used in the study “may impact on your training” but that the results would need to validated for lower doses of simvastatin and in other statins. In addition, he said, the results of a study in a population that does not have established cardiovascular disease should not be extrapolated to people with established disease, in whom the benefits of statins have been conclusively demonstrated.
Leona Rubin, professor in the Department of Biomedical Sciences in the College of Veterinary Medicine, has been named interim dean of the University of Missouri's Graduate School.

Rubin, who has been a professor at MU since 1989, will begin serving as interim dean effective June 1. MU officials will begin a search for a permanent dean soon.

Rubin replaces George Justice, who served as the Graduate School dean since 2010. Earlier this year, Justice announced he would be leaving the position effective June 1 to take the position of dean for humanities in the College of Liberal Arts and Sciences at Arizona State University.

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Crews are working to silence a new noise emitting from the University of Missouri power plant, but it might take awhile.

Karlan Seville, a spokeswoman for MU Campus Facilities, said the source of the high-frequency noise is a fan drive in the cooling tower of the power plant.

“We have been working with the manufacturer for the last month to redesign components that should help reduce the high-frequency noise,” Seville said.

Seville said the noise became noticeable after crews finished vacuuming out biomass from three silos in early April, another noisy process. She said noise readings had been conducted as far as Glenwood Avenue and were within the acceptable noise level for a neighborhood.

Although the problem area has been isolated, she said it will take about three weeks to fix and reinstall each fan, and they must be done one at a time. Seville said the first fan has been taken down and is being equipped with new components; it should be reinstalled by the first week of June.