



Why having surgery later in the day might be better for your health

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The time of day of your surgery could have long-term impacts on your health. That's according to researchers who looked at the way circadian rhythm — the body's internal clock — affects the outcomes of a patient recovering from a complex heart procedure.

Patients who underwent open-heart surgery in the afternoon experienced better health outcomes compared to those who got operated on in the morning, study authors found after six years of observing nearly 600 patients who underwent heart valve replacement. In the subsequent 500 days after surgery, researchers found, those patients who had surgery after noon had half the risk of a major cardiac event — for instance myocardial infarction, acute heart failure, or death — as those who had surgeries before then.

The team also conducted a randomized controlled trial of 88 different patients who got the same surgery, half in the morning and the other half in the afternoon. They found that afternoon surgeries resulted in lower levels of myocardial ischaemia-reperfusion injury — tissue damage that occurs when blood flows again through the repaired portion of the heart — than did morning surgeries. Experts say that sort of heart tissue injury can lead to higher risk of short- and long-term mortality. Results **were published** Thursday in the *Lancet*.

University of Lille-France professor David Montaigne, the study's lead author, suggested that the study's findings indicate that scheduling changes could decrease injury or death.

“There are few other surgical options to reduce the risk of post-surgery heart damage, meaning new techniques to protect patients are needed,” Montaigne said in a statement. “Our findings suggest this is because part of the biological mechanism behind the damage is affected by a person's circadian clock and the underlying genes that control it.”

The findings are the latest in a growing body of evidence suggesting that time of day plays an important role in how well various medical treatments work. Studies show that the efficacy of some **vaccines** and **cancer treatments** may be affected by the time of day when a therapy is administered or medicine is taken. For example, research has found that patients who received a seasonal flu vaccination before 11 a.m. produced more antibodies than those who had one after 3 p.m.

“This study underscores the importance of the circadian rhythm biology that’s finally starting to gain recognition in science,” said James Olcese, a biomedical sciences professor at Florida State University’s College of Medicine who was not involved in the study. “This could potentially save a lot of lives. It’s pretty critical, taking it beyond a basic concept of tissue all the way to the real-world scenario of surgeries occurring at different times of day.”

In this case, the study authors said, differences in gene expression over the course of a day may cause a person’s heart to heal more quickly in the afternoon than in the morning.

The researchers isolated heart tissue samples from a subgroup of 30 patients from the randomized controlled trial. In laboratory tests, tissue from afternoon surgeries more quickly regained its ability to contract when researchers imitated the process of the heart refilling with blood as surgery concludes. Additionally, researchers found that nearly 300 genes showed variation in their expression in heart tissue over the course of a day — a possible basis for the tissue’s change in behavior.

Finally, scientists wanted to test whether they could trick heart muscle into healing in an afternoon fashion regardless of time of day. To do this, they chose a gene that differed greatly in circadian expression — higher in

the morning, much lower in the afternoon — called Rev-Erb α . They studied what happened in mouse hearts when they artificially removed that gene, either by editing it out of the genome or by giving mice a drug to block its effects. And researchers found that, indeed, mice given the drug, or with the gene removed, could recover from morning surgery (mice mornings being nighttime, since they are nocturnal) with fewer side effects than usual.

Developing drugs that modulate genes like Rev-Erb α could therefore help protect human hearts during surgery.

“One could imagine, quite rapidly, a pharmacological approach that could basically wipe out the effects between morning and afternoon,” said University of Lille-France professor Bart Staels, one of the study’s authors.

As to the question, though, of whether patients should change the timing of their own surgeries, the experts offered diverging opinions. “Even before we have drugs available to regulate the circadian clock, one might propose that high-risk patients should preferentially be operated on in the afternoon,” Dr. Thomas Bochaton and Dr. Michel Ovize, both French cardiologists, wrote in an editorial released alongside the study Thursday.

For now, Staels believes that it’s “totally impossible to abandon surgery in the morning.” But if the highest-risk patients can be identified, “you wouldn’t schedule them for morning operation.”

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