

## SSRIs Linked to Bleeding Risk, Death in Surgical Patients

Perioperative use of selective serotonin reuptake inhibitors (SSRIs) has been linked to an increased risk of bleeding, transfusion, hospital readmission, and death, new research shows.

A large retrospective study that included 375 US hospitals and more than half a million adult patients showed that receiving SSRIs in the perioperative period is associated with a higher risk for adverse events.

"There have been small studies that suggested there was a problem, but it has never been well-proven. With this huge dataset, we feel confident in saying that SSRIs are associated with about a 10% increased risk for these adverse outcomes," lead investigator Andrew D. Auerbach, MD, MPH, University of California, San Francisco, said in a release.

The study was [published online](#) April 29 in *JAMA Internal Medicine*.

Among the most commonly prescribed medications in the United States, the researchers note that SSRIs have previously been associated with a "small but elevated risk for hemorrhage," especially when taken in combination with nonsteroidal anti-inflammatories or warfarin. This is thought to be due to the drugs' antiplatelet effects

They add that SSRIs have also been linked to a higher risk for arrhythmias and sudden death in ambulatory patients.

The investigators also point out that SSRIs have been associated with bleeding and adverse outcomes in surgical patients. Similarly, the drugs have also been linked to increased bleeding risk in coronary bypass surgery and orthopedic surgical procedures.

However, they add that determining the risk of bleeding and other adverse outcomes associated with SSRIs has been hampered by a lack of multicenter studies or trials that include a broad range of surgical procedures or surgeons. In addition, few studies were large enough to compare rare outcomes, such as bleeding or mortality.

The investigators also note that patients receiving SSRIs are more likely to have condi-

tions such as obesity, chronic obstructive pulmonary disease, and depression that in themselves increase surgical risk.

To determine whether perioperative use of SSRIs is associated with adverse surgical outcomes, the investigators conducted a retrospective study in a national sample of 530,416 adult patients who underwent major surgery and compared outcomes in patients who were, and were not, taking SSRIs.

The study's primary outcome measures included in-hospital mortality, length of stay, readmission at 30 days, bleeding events, transfusion, and incidence of ventricular arrhythmias.

Of the total sample, 72,540 (13.7%) received an SSRI perioperatively. The most commonly used SSRI was sertraline, followed by escitalopram, fluoxetine, paroxetine, citalopram, and fluvoxamine.

Results showed that compared with non-SSRI users, patients who received SSRIs perioperatively had higher overall mortality (adjusted odds ratio [AOR], 1.20; 95% confidence interval [CI], 1.07 - 1.36), higher 30-day readmission (AOR, 1.22; 95% CI, 1.18 - 1.26), and higher odds of bleeding (AOR, 1.09; 95% CI, 1.04 - 1.15).

"Our results suggest that SSRIs are associated with a range of poorer outcomes after major surgery," the authors write.

They add that although holding SSRI therapy at the time of surgery may be an appropriately conservative approach, the current data "cannot frame a more tailored or nuanced strategy for management in surgical patients receiving SSRIs."

Only a prospective study with multiple arms will be able to determine the question of optimal management for surgical patients taking SSRIs, the researchers note.

"Such a study would be quite costly, but given the ubiquitous nature of SSRIs in US health care and the potential risks of proceeding without adequate evidence for a strategy on how to mitigate risks of perioperative SSRI use, any study costs would seem money well spent," they write.

## To Hold or Not to Hold

In an [invited commentary](#), Marko Mrkobrada, MD, and Daniel G. Hackam, MD, from Western University in London, Ontario, Canada, write that the study authors "should be congratulated for their approach to this largely unexplored question."

However, they add that owing to the study's observational nature, the findings are not practice-changing.

"Even if a causal relationship exists, the number needed to harm is quite large, and thus the attendant increase in absolute risk for the average patient would be very small. Conversely, the cessation of SSRI therapy before surgery may precipitate a discontinuation syndrome, worsen depression, and increase sensitivity to postoperative pain.

"Physicians should continue to initiate SSRI therapy only when clinically indicated. Internists, anesthesiologists, and surgeons should be aware of potential bleeding risks in patient receiving SSRIs in the perioperative setting. Overall, however, we do not believe the evidence base has evolved sufficiently to confirm that patients should routinely have their SSRI therapy tapered or discontinued before surgery," the editorialists write.

*The authors, Dr. Mrkobrada, and Dr. Hackam report no relevant financial relationships.*

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