

Patient Safety Tip of the Week

March 29, 2022

Disturbing Stats on Perioperative Benzodiazepine Use in Elderly Patients

One of the most well-recognized risk factors for delirium in elderly patients is use of benzodiazepines. So, some recent statistics about perioperative benzodiazepine use in elderly surgical patients are particularly troublesome.

Cozowicz et al. analyzed a database of almost 3 million patients undergoing total knee or hip arthroplasty from 2006 to 2019 ([Cozowicz 2022](#)). Benzodiazepine use on the day of surgery occurred in 80.5% of TKA's (72.6% short-acting and 7.9% long-acting) and 76.1% of THA's (68.4% short-acting and 7.7% long-acting). Midazolam was by far the most frequently used benzodiazepine (89.5%), with lorazepam, diazepam, alprazolam, and clonazepam each less than 3%. Benzodiazepine use increased from 2006, peaking in 2011, then decreasing to just below 2006 levels by 2019.

While short-acting benzodiazepines were predominant, long-acting formulations were administered in approximately 8% of cases. Benzodiazepine use was also associated with significantly increased opioid consumption, especially in patients receiving long-acting benzodiazepines. Benzodiazepine use was more frequent in “younger” patients (median age 69!).

The authors note that, despite growing evidence and several guidelines supporting cautious use of benzodiazepines, the persistent high utilization rate across the 14-year study period is surprising, especially given the increasing number of elderly patients receiving THA and TKA. Use of long-acting benzodiazepines is known to be associated with higher rates of postoperative delirium. They also note a disturbing association of increased opioid use in patients receiving benzodiazepines.

The authors call for future research to provide evidence-based guidelines on appropriate use and indications for benzodiazepines in the perioperative period.

A second study looked at the association between perioperative medication use and postoperative delirium and cognition in adults ≥ 70 years without dementia undergoing elective noncardiac surgery ([Duprey 2022](#)). While hospitalized, patients were assessed

daily for delirium using the CAM (Confusion Assessment Method) and a validated chart review method. Cognition was evaluated preoperatively and 1 month after surgery using a neurocognitive battery. Among 560 patients enrolled, 134 (24%) developed delirium during hospitalization. While prehospital benzodiazepine use was not associated with post-op delirium, postoperative hospital benzodiazepine use was associated with greater delirium (adjusted hazard ratio 3.23). But association between in-hospital, postoperative medication use and cognition at 1 month, independent of delirium, was not detected.

Neither study was able to determine the incidence of frailty in their population undergoing the elective surgical procedures. A recent meta-analysis ([Gracie 2021](#)) of articles on patients who were undergoing elective, non-emergent inpatient surgery confirmed a significant association between preoperative frailty and postoperative delirium in elective surgical patients age 65 years or older. It would be of interest to know whether the presence of frailty further increases the risk of postoperative delirium in patients receiving perioperative benzodiazepines.

An interesting study analyzed risk factors for postoperative delirium in critically ill patients in the surgical ICU ([Chaiwat 2019](#)). Of 250 patients enrolled, delirium was found in 61 (24.4%). Independent risk factors for delirium were age, diabetes mellitus, severity of disease (SOFA score), perioperative use of benzodiazepine, and mechanical ventilation. They then developed a predictive score, weighting each of those 6 variables. That predictive score had a sensitivity of 72.13% and a specificity of 80.95% at their suggested cut point. Note that hospital mortality rate was significantly greater among the delirious than the non-delirious patients (25% vs. 6%).

Sharon Inouye, one of the world's leading delirium researchers and key architect of HELP (Hospital Elder Life Program), described a case of postoperative delirium in a *New England Journal of Medicine* "Perspective" – the patient was her own father ([Inouye 2020](#)). She discussed the multiple contributing factors and fact that multiple caregiver teams "each prescribed many drugs to address his ailments, seemingly without consideration of drug interactions, renal dose-adjustment protocols, or his heightened sensitivity to psychoactive drugs". At one point, he was on more than 20 medications, including a benzodiazepine for sleep and several other drugs with psychoactive effects. Asking herself whether her father's delirium could have been prevented, she responds "I believe so. Indeed, all the precipitating factors were potentially reversible or remediable. Yet I realized that no person working alone — not even a delirium expert — can prevent delirium. It takes an enlightened, coordinated health care system with motivated interdisciplinary health care professionals working together to improve care for older adults." Delirium prevention truly requires a coordinated system with all healthcare workers working together.

Managing delirium is difficult, so preventing it is of utmost importance. Exposure to benzodiazepines is one of the contributing factors that all healthcare workers must recognize in elderly patients undergoing surgery.

Some of our prior columns on delirium assessment and management:

- October 21, 2008 “[Preventing Delirium](#)”
- October 14, 2008 “[Managing Delirium](#)”
- February 10, 2009 “[Sedation in the ICU: The Dexmedetomidine Study](#)”
- March 31, 2009 “[Screening Patients for Risk of Delirium](#)”
- June 23, 2009 “[More on Delirium in the ICU](#)”
- January 26, 2010 “[Preventing Postoperative Delirium](#)”
- August 31, 2010 “[Postoperative Delirium](#)”
- September 2011 “[Modified HELP Helps Outcomes in Elderly Undergoing Abdominal Surgery](#)”
- December 2010 “[The ABCDE Bundle](#)”
- February 28, 2012 “[AACN Practice Alert on Delirium in Critical Care](#)”
- April 3, 2012 “[New Risk for Postoperative Delirium: Obstructive Sleep Apnea](#)”
- August 7, 2012 “[Cognition, Post-Op Delirium, and Post-Op Outcomes](#)”
- February 2013 “[The ABCDE Bundle in Action](#)”
- September 2013 “[Disappointing Results in Delirium](#)”
- October 29, 2013 “[PAD: The Pain, Agitation, and Delirium Care Bundle](#)”
- February 2014 “[New Studies on Delirium](#)”
- March 25, 2014 “[Melatonin and Delirium](#)”
- May 2014 “[New Delirium Severity Score](#)”
- August 2014 “[A New Rapid Screen for Delirium in the Elderly](#)”
- August 2014 “[Delirium in Pediatrics](#)”
- November 2014 “[The 3D-CAM for Delirium](#)”
- December 2014 “[American Geriatrics Society Guideline on Postoperative Delirium in Older Adults](#)”
- June 16, 2015 “[Updates on Delirium](#)”
- October 2015 “[Predicting Delirium](#)”
- April 2016 “[Dexmedetomidine and Delirium](#)”
- April 2016 “[Can Antibiotics Lead to Delirium?](#)”
- July 2016 “[New Simple Test for Delirium](#)”
- September 20, 2016 “[Downloadable ABCDEF Bundle Toolkits for Delirium](#)”
- January 24, 2017 “[Dexmedetomidine to Prevent Postoperative Delirium](#)”
- March 21, 2017 “[Success at Preventing Delirium](#)”
- July 2017 “[HELP Program Reduces Delirium Rate and LOS](#)”
- January 2018 “[What Happens After Delirium?](#)”
- February 20, 2018 “[Delirium and Falls](#)”
- October 2018 “[Rapid Screening for Delirium](#)”
- November 13, 2018 “[Antipsychotics Fail in ICU Delirium](#)”
- February 12, 2019 “[2 ER Drug Studies: Reassurances and Reservations](#)”
- September 17, 2019 “[American College of Surgeons Geriatric Surgery Verification Program](#)”
- March 2021 “[The Fiscal Costs of Delirium](#)”
- March 16, 2021 “[Sleep Program Successfully Reduces Delirium](#)”

- January 4, 2022 “[Spin or Not: A Useful Secondary Finding in a Study](#)”
- February 1, 2022 “[Perioperative Delirium is Not Just Postoperative](#)”

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[https://journals.lww.com/anesthesia-analgesia/Abstract/2022/03000/The Perioperative Use of Benzodiazepines for Major.9.aspx](https://journals.lww.com/anesthesia-analgesia/Abstract/2022/03000/The_Periooperative_Use_of_Benzodiazepines_for_Major.9.aspx)

Duprey MS, Devlin JW, Griffith JL, et al. Association Between Perioperative Medication Use and Postoperative Delirium and Cognition in Older Adults Undergoing Elective Noncardiac Surgery. *Anesthesia & Analgesia* 2022; Published ahead of print February 24, 2022

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