Discussion of 2021-1735

PREOPERATIVE OPIOID DOSE AND SURGICAL OUTCOMES IN COLORECTAL SURGERY

**DR JOHN MIGALY** (Durham, NC): As a brief overview, the authors use the MarketScan database in a retrospective study of more than 45,000 patients receiving elective colon surgery and examined the rate of complication as compared with the average daily preoperative milliequivalents of morphine use over a 90‑day period before operation. Through multivariate analysis, the authors were elegantly able to demonstrate an escalating dose relationship between preoperative morphine use and odds of anastomotic leakage as their main endpoint, but they also demonstrated increased lung complication, pneumonia, delirium and 30‑day readmission.

Could the authors please elaborate on how they chose the 3 numerical cohorts of morphine equivalence of 0, 1 to 49, and greater than 50? I am particularly interested in the wide range of the middle group of 1 to 49. I do not disagree with this, but another way to look at this data would be to not assume a linear relationship between dose and complication and use other statistical methods, such as restricted splines, to see if there is an inflection point, ie a dose of morphine above which the complication rate rises.

Secondly, while the MarketScan database has the power of numbers, it does not by design have the granularity of an institutional database or the electronic medical record. Could it be possible that the morphine equivalence could be a proxy for disease severity, and could data on hypoalbuminemia, preoperative enteral parenteral nutritional supplementation, Eastern Cooperative Oncology Group (ECOG), Karnofsky performance status score, or some other administrative billing equivalent to that, have been additive to your multivariate analysis?

Lastly, the authors posited deleterious downstream effects of morphine misuse on the immune response most or, most likely, in my opinion, on the gut microbiota. Should we be attempting to prehabilitate this patient population, and is there any given example in your institution, or otherwise, of prehabilitation of morphine use being used?

It is, in rectal cancer surgery, an ideal disease process along with diverticular disease and inflammatory bowel disease (IBD), as there is a defined and reasonable timeframe to perform morphine prehabilitation.

**DR STEVEN R HUNT** (St Louis, MO): Over the last several years, we have all become acutely aware of the ravages of the opioid epidemic, and some of us have been forced to acknowledge at least some culpability in contributing to this problem. I want to thank Dr Safar and his group for this eye‑opening study. It also gives us some insight into the role that opioid use may play in the operative outcomes of our patients. I think most of us see preoperative opioid use as an issue that will affect pain control in the postoperative period, but now we can also see it as something that may contribute to some of our most serious complications. The authors have used a powerful database to demonstrate that preoperative opioid use is associated with a significant increase in anastomotic leak, pulmonary complication, and a doubling of the rate of readmission.

As the authors cannot account for opioids that are illicitly obtained, and because the database includes only private insurance patients, the magnitude of the problem is likely much worse. While I can understand why a chronic opioid user may have difficulty with postoperative pain control and decreased mobility that may contribute to some of these complications, such as pulmonary outcomes, I have more difficulty understanding why opiates alone would contribute to anastomotic leak. The patients in this study have diseases that may predispose them to malnutrition.

Additionally, preoperative opioid use may just be a surrogate for bad disease. The Charleson Comorbidity Index does not really account for malnutrition or severity of disease. Getting insight into these types of issues in a large database is extremely difficult. I wonder if the authors have any thoughts as to how we might account for these confounders in a future study. Also, I would imagine that some of the patients in your study are on chronic opioids for unrelated problems, while some are using opioids to address the pain from their IBD, diverticulitis, or cancer. Frequently, these patients just need a short course of opioids as a bridge to surgery. From your database, can you tell how long this exposure to opioids is necessary before we begin to see these untoward outcomes?

Finally, this study makes it clear that screening for opioid use should be an important part of preoperative assessment. As surgeons, we are not very good at weaning patients from opioids except to simply cease prescribing them. For long‑term opioid users, just saying no is not really a solution.

Suboxone is frequently prescribed as medical therapy for opioid abuse and may be the only effective treatment. It is also a drug that can make it extremely difficult to manage pain in the postoperative period.

Were you able to differentiate Suboxone? I did not see it on your list, and do you think that that might have had any effect on any of these patients in these outcomes?

**DR JONATHAN LARYEA** (Little Rock, AR): There is data that perioperative opioid dosage is associated with worse outcomes. Do you think that preoperative opioid use is a surrogate for perioperative dosing of opioids, and does your database account for that? In other words, do patients who use opioids preoperatively tend to get higher perioperative doses of opioids, which has been associated with worse outcomes?

**DR SUSAN L GEARHART** (Baltimore, MD): This study examines preoperative opioid use, but changes in opioid use that have occurred in colorectal surgery over the past 10 years have affected perioperative use. We are beginning to investigate how implementation of enhanced recovery programs have affected perioperative opioid use, especially in our patients who come in on opioids (opioid tolerant). Perhaps there is an opportunity to look at this data over time and trend their outcomes to see if our widely implemented programs, such as enhanced recovery after surgery (ERAS) has influenced postoperative outcomes, particularly for patients on opioids.

**DR WILLIAM C CHAPMAN** (St Louis, MO): You show that increased opioid use is associated with increased complication the patients and in their postoperative period, but you also show that these patients are more complicated. They are sicker patients. They are not the same group. So, can you conclude that reducing opioid use is going to reduce complication?

**DR BASHAR SAFAR** (Baltimore, MD): We chose the morphine milligram equivalents (MMEs) from 0, 1 to 49, and then above 50 was considered a high dose and associated with high risk of complication. We decided to evaluate the patients who were not on opioids at all, who were the vast majority of our patients; patients who were not high-dose and patients who were high-dose. The number of high-dose patients dropped significantly, so that even if we went to 90, there would have not been very many patients in that cohort. So, above 50 was where we decided to cut it off.

The question regarding comorbidity and the outcomes is obviously a valid one. We tried to adjust for that in multivariate analysis, and we looked at the risk factors that could show what was significant. When we ran the multivariate analysis, it still showed that the opioid dose was significant ‑ it was statistically associated with anastomotic leak. So, even though we cannot conclude with any certainty, we feel that this is a good start. Now, again, this database is not exactly granular, so this study could and probably should be repeated, as Dr Gearhart mentioned, in some institutional databases and/or through the College, where we look at ERAS programs. In our program, for example, because we already instituted ERAS, we have an answer to another question: we have a prehabilitation clinic, which was funded last year as R01. But on our anesthesiology team, all patients who come into surgery on high-dose opioids, the goal is to switch them to multimodality.

The 90-day cutoff was based on the CDC guidelines: you must reassess the opioid dose at 90 days. I suppose 90 days could be considered a short time to be labeled chronic opioid use. We wanted to look at patients who were coming into surgery having been on a high dose within 90 days, almost by coming into surgery having been on steroids for 90 days and see if that made any difference.

As for Suboxone, we did include that in our analysis because we felt it was a complex opioid; because it is used in combination with Naloxone, and I agree, it makes postoperative pain management very difficult. Is being on the highest opioid dose a surrogate for increased morbidity or increased complexity of the disease process? Absolutely, but the data does not allow us to find that exact variable.