

is defined as “sets of information that are too large or too complex to handle, analyze or use with standard methods.” Finally, a robot is considered as “a machine that can perform a complicated series of tasks by itself.”

Once reading the definitions, one understands that artificial intelligence is the overall entity that researchers have used to build robots, and that machine learning enables the robot to “evolve” itself, adapting and adjusting to perform better using its own experiences. In a recent review article on artificial intelligence,<sup>3</sup> the importance of input by practicing clinicians in the further development of devices using artificial intelligence was pointed out: one could imagine that future robots will be put into use and that they might “improve” on the job, as humans should do, using machine learning based on experiences, feedback from the clinicians, and program changes. Big data will be helpful because the more “data” are available, the more the robot can use to improve: big data are the computer equivalent of years of experience of a human anesthesiologist.

Obviously, robots improving on their own using machine learning will be a significant challenge not only for the developers but also for regulatory entities, which will have to “recertify” or “re-evaluate” these robots. It is also important to notice that machine learning is still in its infancy with some research in anesthesia showing promising results. Arora<sup>1</sup> states that machine learning algorithms are capable to outperform human decision-making provided that their data set is reliable. I personally believe that machine learning will “take off” with the widespread creation of big data and its use to develop appropriate machine learning algorithms. The more data can be fed into a machine learning system, the better this system can adapt. To repeat the former analogy, the more experience an anesthesiologist has, the more he or she has experienced, and his or her techniques have been able to evolve and change. I believe that future developmental strategies should adopt a concept where new big data are constantly fed into a robot in order for it to improve itself, similar to anesthesiologists who grow wiser and better with years of training, training in simulation, reading books and articles... This concept could be a sort of “continuous medical education” for robots!

### Competing Interests

The author declares no competing interests.

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## Methadone and Chronic Pain: Comment

### To the Editor:

I read with interest the article by Murphy *et al.*<sup>1</sup> Their study was thought provoking in the context of reducing postoperative medication requirements in the midst of our nation’s opioid crisis. I was most interested in the results of the complex back surgery patients and their postoperative pain medication use.

Preoperative opioid use is not documented in their study. Previous studies have shown that preoperative use of opioids is one of the most important risk factors in long-term opioid use postoperatively.<sup>2</sup> Without knowing which patients were taking preoperative opioids, it is difficult to interpret their postoperative analgesic requirements and frequency of use results.

This study examines the very interesting idea of adding perioperative methadone to reduce postoperative analgesic requirements. I am encouraged that the authors are pursuing innovations in enhanced recovery after surgery protocols to minimize postoperative pain and opioid use.

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The author declares no competing interests.

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## Methadone and Chronic Pain: Reply

### In Reply:

We thank Dr. Romanoff<sup>1</sup> for his interest in our study of postoperative pain and analgesic requirements in the first year after intraoperative methadone for complex spine and cardiac surgery.<sup>2</sup> Although the study was neither designed nor powered to determine the relationship between preoperative opioid use and postoperative analgesic requirements, we attempt to address his concerns with *post hoc* analyses.

Exclusion criteria for the study of intraoperative methadone for the prevention of postoperative pain in cardiac surgery patients included use of preoperative opioids or recent history of opioid abuse.<sup>3</sup> Thus, preoperative opioid use could have no effect on their postoperative analgesic requirements.

Although the exclusion criteria for the study of intraoperative methadone in patients undergoing posterior spinal fusion surgery included preoperative use of methadone or hydromorphone and a recent history of opioid abuse,<sup>4</sup> 16 of the 27 (59%) patients in the hydromorphone group and 20 of the 39 (51%) patients in the methadone group for whom data were available at 3 months follow-up had taken opioids by prescription preoperatively (risk difference [99% CI], 7% [–25 to 36%]; Yates corrected chi square  $P = 0.782$ ). Seven of the 11 (64%) patients in the hydromorphone group requiring analgesic medication at 3 months had taken opioids preoperatively, whereas one of the four (25%) patients in the methadone group requiring analgesic medication at 3 months had taken opioids preoperatively (risk difference

[99% CI], 39% [–32 to 80%]; Fisher's exact test  $P = 0.282$ ). Seven of the 16 (44%) patients in the hydromorphone group taking opioids preoperatively required analgesic medication at 3 months, whereas four of the 11 (36%) patients not taking opioids preoperatively did (risk difference [99% CI], 7% [–40 to 50%]; Fisher's exact test  $P > 0.999$ ). One of the 20 (5%) patients in the methadone group taking opioids preoperatively required analgesic medication at 3 months, whereas three of the 19 (16%) patients not taking opioids preoperatively did (risk difference [99% CI], –11% [–42 to 20%]; Fisher's exact test  $P = 0.342$ ).

Thus, although the study was not powered to detect differences in the variables being tested in these *post hoc* analyses, the results suggest that there were no differences between the hydromorphone and methadone groups in either the proportion of patients who had taken opioids preoperatively or the proportion of patients who had taken opioids preoperatively requiring analgesic medication at 3 months. These analyses also suggest that there were no differences in the proportion of patients who took opioids preoperatively and required analgesic medication at 3 months and the proportion of patients who did not take opioids preoperatively and required analgesic medication at 3 months in either the hydromorphone or methadone groups.

### Competing Interests

Dr. Murphy has served as a speaker for Merck (Kenilworth, New Jersey). Dr. Avram is the Assistant Editor-in-Chief of *ANESTHESIOLOGY* (Schaumburg, Illinois). Dr. Szokol declares no competing interests.

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## Blood Pressure Components and Organ Injury: Comment

To the Editor:

We read with great interest the article by Ahuja *et al.*<sup>1</sup> on the association between various intraoperative blood pressure components and postoperative morbidity. They identified an association among the arterial systolic, mean, and pulse pressure hypotension with myocardial and renal injury. Although the main finding—a lower blood pressure can be associated with postoperative myocardial injury after noncardiac surgery and acute kidney injury—offers clinically valuable information, we believe that some inherent bias in the study design should be discussed and clarified.

First, compared with previously published studies, this study had an important difference in the definition of myocardial injury after noncardiac surgery.<sup>2</sup> The outcome definition of myocardial injury in this study (*i.e.*, elevation of troponin or creatinine kinase-myocardial bound during the first 7 postoperative days)<sup>1</sup> was different from that approved by the consensus diagnostic criteria in 2014, which defined myocardial injury after noncardiac surgery as “elevated post-operative troponin measurement judged as resulting from myocardial ischemia during or within 30 days after non-cardiac surgery.”<sup>3,4</sup> In addition, this study did not exclude nonischemic etiologies (sepsis, arrhythmias, pulmonary embolism, *etc.*). A previous study showed that elevation of troponin levels in 11 to 14% cases after noncardiac surgery was due to nonischemic etiologies.<sup>3</sup> Therefore, without an adequate outcome assessor, the results of Ahuja *et al.*<sup>1</sup> tend to overestimate the actual incidence of myocardial injury by including nonischemic etiologies. Although this exclusion was not possible because of the retrospective study design using electronic medical records, the authors should discuss this aspect in the study limitations.

Second, residual confounding might have been present because compared with routine postoperative biomarker screening, the postoperative measurements of cardiac biomarkers were likely to be influenced by clinical indication (“confounding by indication”).<sup>5</sup> As stated by the authors, the postoperative troponin concentration was measured in only 25% of the samples, and the authors assumed that myocardial injury was absent in patients without troponin surveillance.<sup>1</sup> This assumption can induce serious outcome detection bias. In clinical practice, postoperative cardiac biomarkers (troponin or creatinine kinase-myocardial bound) are not measured routinely. Results of previous studies indicate that majority of the patients with myocardial injury after noncardiac surgery (approximately 90%) do not have clinical cardiac symptoms and are not surveilled for troponin measurement.<sup>6,7</sup> Therefore, measurement of postoperative cardiac biomarkers was mostly restricted to only high-risk patients or those with clinical signs of myocardial ischemia.<sup>8</sup> In addition, differential surveillance for outcome assessment in patients who experienced or did not experience intraoperative hypotension can induce surveillance bias.<sup>9,10</sup> If possible, Ahuja *et al.* should perform sensitivity analyses in patients who undergo troponin surveillance (5,699 patients) to test the robustness of their results. This information will be valuable to the readers of *ANESTHESIOLOGY*.

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The author declares no competing interests.

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