Host: Welcome to the Anesthesiology journal podcast, an audio interview of study authors and editorialists.

Dr. James P. Rathmell: Hello. I'm Jim Rathmell, professor of anesthesia at Harvard Medical School and chair of the Department of Anesthesiology, Perioperative and Pain Medicine at Brigham and Women's Hospital. I'm one of the executive editors for Anesthesiology, and you're listening to an Anesthesiology podcast that we've designed for physicians and scientists interested in the research that appears in the journal. Today we're going to talk with the senior author of an original research article and the author of an accompanying editorial that appear in the August 2021 issue.

With us today is Dr. Alexandre Joosten. Dr. Joosten is a consultant in anesthesiology and a clinical researcher at Université Paris-Sud, Hôpital de Bicétre in Le Kremlin-Bicétre, France. And I probably didn't do that justice. Dr. Joosten is the first author on an article that appears in the August 2021 issue of the journal, and that's titled "Computer-Assisted Individual Hemodynamic Management Reduces Intraoperative Hypotension in Intermediate and High-risk Surgery: A Randomized Controlled Trial." Dr. Joosten, thank you for joining us.

Dr. Alexandre Joosten: Hello, Dr. Rathmell and Story, and thank you very much for the invitation.

Dr. James P. Rathmell: We also have with us today Dr. David Story. Dr. Story is a professor of anesthesia and head of the Department of Critical Care at the University of Melbourne in Melbourne, Australia. Dr. Story authored an editorial that accompanies Dr. Joosten's original research article, and it also appears in the August 2021 issue of the journal. And that editorial is titled "Computer-assisted Anesthesia Care: Avoiding the Highway to HAL." Dr. Story, welcome and thank you for joining us.

Dr. David Story: Thank you very much, Dr. Rathmell. And hello, Dr. Joosten.

Dr. James P. Rathmell: Dr. Joosten, congratulations on the publication of your study. Let's set the stage for listeners by reading a few sentences from the introduction of your manuscript. You tell us, '"Individualized hemodynamic management during surgery relies on accurate titration of vasopressors and fluids, and computer systems have been developed to assist anesthesia providers in delivering these interventions."

So you and your research team set out to test one of these new computerized systems to manage hemodynamics during surgery. What was the original hypothesis of your study?

Dr. Alexandre Joosten: So our original hypothesis of our randomized controlled study was to demonstrate that patients managed using the computer-assisted system for both fluid and vasopressor administration would experience less intraoperative hypotension when compared to patients in whom vasopressors and fluid administration were adjusted manually.

Dr. James P. Rathmell: Can you described the computerized system you used? The system was coupled with a decision support system for fluid management that incorporated machine learning algorithms to make suggestions to the anesthesiologist about fluid administration. So there's two systems, and I want you to try and help listeners understand how these two systems were used together.

Dr. Alexandre Joosten: Yes. Of course. So we used two different systems from one single hemodynamic monitoring device, so a decision-support system that recommend to the clinician when to administer a bolus of fluid. Then the system can analyze the effect of the bolus of fluid on stroke volume and stroke volume variation and then continuously reassess the patient's status for further fluid requirement. This decision-support system is called assisted fluid management system, and it's incorporated into the EV1000 clinical platform of Edwards Lifesciences.
And from the same monitor, we also extract the MAP, mean arterial pressure, values and then use an automated closed-loop system to titrate a norepinephrine infusion in order to maintain a mean arterial pressure target within a narrow range. So we optimized both stroke volume and mean arterial pressure using such computer-assisted systems.

Dr. James P. Rathmell: Now, tell us how you designed the study to test the computerized hemodynamic system against more traditional ways of managing hemodynamics. And then what was the primary outcome measure you used?

Dr. Alexandre Joosten: Yes. So you – we all know that in 2017 Emmanuel Futier published in JAMA a large multicenter study which reported that individualized blood pressure management reduces organ dysfunction compared to standard of care in patient undergoing major surgery. So in my hospital, in Bicétre Hospital in January 2019, a group of five anesthesia team leaders worked closely with the chairman of our department, Jacques Duranteau, in order to design a individualized hemodynamic protocol to rationalize the way fluid management and hemodynamic optimization are conducted during major surgery. So for fluid management, the protocol consisted in baseline fluid administration an additional mini-fluid challenge in order to optimize stroke volume. And for blood pressure control, the goal was to maintain mean arterial pressure within 10% of patient baseline value.

And as you may imagine, this strategy requires constant monitoring and optimization of both stroke volume and mean arterial pressure, and this was not so easy to implement. And I personally think that simply being surrounded by hemodynamic monitoring and having an established hemodynamic protocol does not ensure that fluid and vasopressors will be well titrated to all patients because there must also be appropriate and timely interpretations and interventions.

And to overcome this issue, I have developed with some colleagues from California automated closed-loop system for both fluid and vasopressor infusions. And so we decided to compare both strategies, manually conducted fluid and vasopressor titration versus a computer-assisted fluid and vasopressor titration. And our primary outcome was intraoperative hypotension defined as the percentage of intraoperative case time patients spent with a mean arterial pressure below 90% of patient baseline value.

Dr. James P. Rathmell: Okay. So just to repeat that, the primary outcome measure was intraoperative hypotension, and that was defined as the percentage of the intraoperative case time that patients spent below 90% of their baseline preoperative blood pressure. And you recorded measurements in 38 patients, 19 in each treatment group. What did you find?

Dr. Alexandre Joosten: We found that patients in the computer-assisted group had significantly less hypotension, 1.2% versus 21.5% in the manually adjusted therapy group.

Dr. James P. Rathmell: Now, that's pretty impressive. So intraoperative hypotension only 1.2% of the time in patients with the computerized-assisted group and 21.5% of the time in the group using an algorithm that was really responded to manually by the anesthesiology or the anesthetist. What were the limitations of your study?

Dr. Alexandre Joosten: So I can see four main limitations. First, of course I supervised the computer system for each patient, randomizing the computer-assisted group, but I was not the primary anesthesia provider. And this was done on purpose because it was requested by the IRB for safety reasons.

Secondly, the primary anesthesia care provider in the control group was not involved in the current study and not author of the current study, and therefore, maybe they can be less focused at optimizing hemodynamic status that is aware of the study purpose. But I have to tell you that individualized GDT protocol was already in place in our institution before the study.

Thirdly, we were unable to record the duration of hypotension during anesthesia induction because our system required post-induction arterial line placement. And, fourthly, our protocol was limited to intermediate to high-risk abdominal and orthopedic surgery. And, therefore, the study findings cannot be extrapolated to other surgeries like cardiac surgery or other clinical settings like intensive care unit patients.

Dr. James P. Rathmell: All right. We'll talk more about the limitations with Dr. Story in just a minute, but I want to ask you one more question. When do you think that computer-assisted hemodynamic management might be available in a form that practicing clinicians can use in various parts of the world?

Dr. Alexandre Joosten: So even if I considered myself as an optimistic person, I think that implementation of such system in clinical practice will take time. There are, of course, many technological, practical, and of course, as you may imagine, regulatory considerations, so I think it will take some time.

Dr. James P. Rathmell: Dr. Story, I want to turn to your editorial. It also appears in the August 2021 issue of the journal, and that editorial is titled "Computer-assisted Anesthesia Care: Avoiding the Highway to HAL." You do a terrific job of putting Dr. Joosten's article into perspective. Can you start by reminding listeners about the story of 2001: A Space Odyssey and the role of the character HAL?

Dr. David Story: Yes. Thank you. So the movie 2001 was made over 50 years ago in 1968 and is widely regarded as one of the greatest movies ever made. And it tells a story of astronauts traveling to Jupiter on a spacecraft, and they have, using the phrase and talking here, computer-assisted. So they're computer-assisted by the HAL 9000, which if you look at the name is quite clever because it's the letter before each of the letters in IBM.

And as they're proceeding, HAL malfunctions for reasons that are unclear and, in fact, kills most of the astronauts. And there's a very famous scene where one of the astronauts has to get back into the spaceship and then deactivate HAL. And he asks HAL to open the door, and HAL says, "I'm sorry. I can't do that."

And so it sends a very strong message about the potential failures and fatal failures of computer-assisted technology, although it's from over half a century ago. And I think with this particular story of failure of computer-assisted, I wanted to just highlight the idea of systems. You know, they can be very good when they work, and they can be very bad when they fail.

Dr. James P. Rathmell: Oh, that's great. Let's get into the details. The computer-assisted closed-loop blood pressure system used in Dr. Joosten's study is a PID type of controller. Can you describe how this type of controller works and any examples of this type of controller that might be more familiar to us in our daily lives?

Dr. David Story: Yes. I might actually answer that question backwards because I think it's easier to use the example to go back to the system. So the best example of this type of controller is cruise control in our cars where we set a speed that we want to be at, and then the car tries to keep us at that speed with reasonable precision.

And, again, as we go back to Dr. Joosten's study, the idea of the precision of the blood pressure was really what we're talking about here. And so we have a system, and it's called PID, which is for the input into the model. It's a widely used engineering model. And I'm the first to say I'm not an engineer, but this is my understanding of the system, that it has different types of input, and they're proportional, integral, derivative, and that's hence the name PID.

So that as there is change – so if we think back to our car analogy, that if you're going up a hill, it requires different inputs. If you're going downhill, it requires different inputs. And the further you get from where you want to be, the more correction. What you don't want is overshoot. In the same way in Dr. Joosten's system and in our care of patients, we want the blood pressure to be what – where we'd like it to be, but what we don't want is overshoot or undershoot as we change what we're doing. We don't want, you know, what is sometimes called the alpine anesthetic. In fact, Dr. Joosten's trying to produce the reverse of that: a very smooth, very precise anesthetic.

Dr. James P. Rathmell: The opposite of a beginning resident, I guess. So why do you think Dr. Joosten and his colleagues found superior hemodynamic performance in the computer-assisted arm of their trial?

Dr. David Story: Well, you know, I think the car analogy works very well because if we look at the data that his group produced, that they found that there was far more incremental changes in management in the computer-assisted arm than there was in the usual care arm. And I think that is the key to so much success. And they had less use of norepinephrine and less use of fluids in their arm, and that is consistent with the idea that one of the advantages of cruise control apart from avoiding speeding fines is better fuel economy. So I think it is that multiple, frequent titrations of effect that lead to a more precise blood pressure in this setting.

Dr. James P. Rathmell: So small, frequent changes. So there seem to be significant benefits of these OR autopilots. What are some of the unintended consequences of using automated systems in the operating room?

Dr. David Story: I think the one that we're all most concerned about – and I would use the analogy of ultrasound-guided central line placement. If we ask one of our residents now—and I've done this several times in the operating room—"How would you feel if you had to put in a central line without an ultrasound?" there's a look of horror on their face. And I think there's the move to having more automated systems and relying on those systems and also believing in those systems. I mean, if we look back to 2001, there's this strong belief that HAL is correct, so the risk of having a bias towards the correctness of the automation and being reluctant to say, "Well, actually, it's wrong. We need to do something different." So there's that bias towards automation.

There's also the inability, then, to manually – to use an aviation analogy, to manually fly the plane or manually manage the patients in an appropriate way. So there's issues around reliance on automation, being unable to deal with a situation if the automation isn't working. And so whilst we would hope overall – and I think one of the things is that when these sort of systems come in, overall things go well. But when things go wrong, they can go badly wrong.

And, you know, we've had two airline crashes within the last few years where it was actually the automated system that was failing rather than the pilots themselves. So I think what we want is to maintain our skills. What we want is to apply the technology appropriately, but we want to avoid overreliance and overexpectation of that technology.

Dr. James P. Rathmell: Yes, the 737 MAX. They – the pilots didn't understand what the plane was trying to do because they were never told, but if they'd just disengaged the autopilot and flew the plane, all would've been well.

So as automated systems come into more common use, what can practicing anesthesiologists and those who run our anesthesiology training programs do to assure that anesthesiologists are prepared to use these automated systems safely and effectively?

Dr. David Story: Well, I think – again, we use the airline analogy in anesthesia very frequently and particularly around simulation. So if we look at that situation with the 737 MAX, if those pilots had had that information and particularly if they'd had the simulation, that may well have avoided those problems. So the important thing is in the same way that civil aviation expects our pilots and then – and also our commercial and military pilots to understand the system they're using, so the inputs, the outputs, how it works, but particularly where it has limitations, we use different technologies where we know that the systems are more unreliable.

And often in the hemodynamic monitoring in the setting of rapid atrial fibrillation, that's one example. So that we understand the limitations and then we also understand how to deal with the situation. And I think over time simulation with the different aspects of these and different types of failures and how to manage them will probably be one of the major training approaches as well as just, if you like, the book learning of knowing what the inputs and the performance of the systems, how they work.

One of the concerns as we bring out new technologies is the black box components of this and what is hidden. I'd like to use an analogy that I think has become important. Recently with the COVID crisis, it's become clear that one of the limitations of pulse oximetry is the way that the devices are calibrated by the manufacturers often excluded people with dark skin, and there's been reports in the literature that patients with really dark skin may have had overestimates of their oxygen saturations when they're profoundly hypoxic.

And this is something that—(sounds like: we've seen the why) in the literature—that has come back to the surface, so we have a limitation with our technology that people weren't particularly aware of because of the way things have developed. So I think we need to – the technology and the inputs and what are freely available to those using that technology to best understand when they work but also why they may be failing.

Dr. James P. Rathmell: Makes sense. So understand the system you're using, the automated system you're using, and then practice with that system in simulated environments so that you can know how to respond when the system isn't working properly. So from your own viewpoint in Australia, when do you think we might see automated systems come into common use in anesthesiology?

Dr. David Story: The second half of the system that Dr. Joosten used, the advisory system rather than the closed-loop system, is now available in Australia and New Zealand. But I think as we move towards the more automated system and particularly since it may be expensive – I mean, one of the – Australia has a lot of our procedures done in public hospitals, and so, you know, the budget is very important. And we're very interested in the cost effectiveness, particularly of new technology. So we want to be confident that we can bring a new technology and that we're using it in the right group of patients, which is in this situation is likely to be patients who are a higher risk because their comorbidities and/or the nature of the surgery that they're having. So we would want to be confident that this technology or this type of technology will improve outcomes.

So I think Dr. Joosten has done a great efficacy study. And coming from an area of the world where we're very strong in pragmatic clinical trials, I would like to see clinical trials of this technology done where we're looking at important end points, including major comorbidity, but also metrics such as days alive and out of hospital and demonstrating that there is improved outcomes with these technologies in the appropriate sets of patients.

That makes us much more confident but also makes it easier for us to debate with those who hold the purse strings about implementing these technologies. If we can confidently say, "Look, we will help these patients, and this will also be of value to the system" – in countries such as Australia, there's a lot of expectation because of fairly central control over the availability of technologies.

Dr. James P. Rathmell: Yes. And something that we probably didn't talk enough about here today is yes, the computer-assisted system was better at maintaining blood pressure within limits, very narrow limits, but did that make any difference in the outcome of patients? Really important to remember.

So, Dr. Joosten, tells us what comes next for you and your research group.

Dr. Alexandre Joosten: Yes. So as you know, we have developed automated systems for fluid administration, and then we shift to vasopressor administration more recently. And, of course, they work independently today, and my long-term vision has always been to integrate both systems into a unified, controlled system that can cross-coordinate activity because, you know, vasopressor and fluid management is naturally comparative combination. We often give both of these drugs, if I can say, simultaneously. So once it's done, then of course we'll have to do a large outcome study, but this will require probably to win a national grant because it will cost a lot of money.

And, finally, the role of machine learning and predictive analytics in automation may also provide opportunities to further improve performance of our system. And we are also today actively working on this topic, so we have some novel paper to come in the near future.

Dr. James P. Rathmell: Terrific. I hope today's discussion will leave many of you listening to read this new article that appears in the August 2020 issue of Anesthesiology, where you can learn more about computer-assisted anesthesia care.

Drs. Joosten and Story, thank you for joining me today and for the terrific explanations.

Dr. Alexandre Joosten: Thank you again for the invitation.

Dr. David Story: Thank you very much.

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