



American Society of
Anesthesiologists™

Central Line
Episode Number 21
Episode Title – Brain Health Revisited

(SOUNDBITE OF MUSIC)

VOICEOVER:

Welcome to ASA's Central Line, the official podcast of the American Society of Anesthesiologists, edited by Dr. Adam Striker.

DR. ADAM STRIKER:

Welcome to another episode of Central Line. I'm Adam Striker, editor and host. Today, we're going to share some curated conversations on the topic of perioperative brain health previously recorded by the ASA, conversations that are vital, informative and can impact your practice. First, Dr. Miles Berger, Assistant Professor of Anesthesiology at Duke University discussed best practices for improving perioperative brain health for older patients with Dr. Stacie Deiner, Professor of Anesthesiology, Perioperative and Pain Medicine at Mount Sinai Hospital. They analyzed four key recommendations for dealing with perioperative neurocognitive disorders, PND. Let's listen in.

DR. MILES BERGER:

Best practices for post-operative brain health are organized around four key issues, uh, pre-procedure consent, preoperative cognitive assessment, intraoperative management and postoperative follow-up. These four issues form the basis of our recommendations.

DR. STACIE DEINER:

Let's start with informed consent. What is the recommendation for best practice?

DR. BERGER:

So our group felt that all patients over the age of 65 should be informed of the risks of perioperative neurocognitive disorders or PND, including confusion, inattention and memory problems after having an operation.

DR. DEINER:

Now, why did your group feel that it was so important to discuss PND as a part of consent?

DR. BERGER:

So we believe that patients should be informed about the risk of perioperative neurocognitive disorders as part of the informed consent for anesthesia and surgery for several reasons. Uh, first, the risk of these perioperative neurocognitive disorders is much more common than other risks that anesthesiologists and surgeons routinely tell patients about, and consent them for, such as the potential of intraoperative mortality or intraoperative awareness with explicit recall.

Uh, second, consenting patients about PND risk gives them a realistic impression of what they're cognitive state may be like in the days, weeks, and months after anesthesia and surgery.

Third, consent allows patients to plan. They can either make important cognitive decisions before anesthesia and surgery, or delay making them until several months afterward when they're more likely to be, uh, at their full cognitive faculties.

Fourth, informing patients of PND risks might even help reduce the risks of these disorders. For example, encouraging family members to talk with the patient and be around them and encourage early mobility could potentially reduce the risk of perioperative neurocognitive disorders.

DR. DEINER:

Dr. Berger, ideally when should these consent discussions occur?

DR. BERGER:

So, ideally, these consent discussions should take place well before the day of surgery, so that patients have a chance to learn about these risks in a less stressful environment. This would also give them time to clarify any issues and ask questions.

DR. DEINER:

Yes, that's an important point. Now let's talk about cognitive assessment, which is the second recommendation for best practice for postoperative brain health.

DR. BERGER:

Yes, so in patients 65 and older, we recommend objectively evaluating a patient's baseline cognition with a brief screening tool during a preoperative evaluation. We also recommend doing a baseline cognition assessment in any patient with risk factors for pre-existing cognitive impairment.

DR. DEINER:

Why is cognitive testing before surgery so important?

DR. BERGER:

So, assessing a patient's baseline cognition is important because preoperative cognitive impairment is a strong risk factor for perioperative neurocognitive disorders. Assessing baseline cognition is also important for informed consent and so patients can make an informed decision about their care.

As anesthesiologists, we currently assess many other organ systems as part of our routine preoperative evaluation through taking a medical history and performing a physical examination. So it makes sense to assess the central nervous system, the brain, uh, before altering it with anesthetic drugs, especially because the central nervous system is the target organ of nearly all anesthetic drugs and analgesic drugs, and plays a central role in perioperative neurocognitive disorders.

Moreover, assessing baseline cognition before surgery can help us identify patients who are at risk for perioperative neurocognitive disorders, including patients with age-related comorbidities such as hypertension, diabetes and or obstructive sleep apnea. If patients are deemed to be at increased risk for perioperative neurocognitive disorders, a preoperative discussion can help them make important decisions before surgery.

DR. DEINER:

Dr. Berger, how should a patient's cognition be assessed prior to surgery?

DR. BERGER:

So, it's not practical or appropriate to conduct a lengthy neuropsychological assessment during a routine preoperative clinic visit. So, we recommend using just a brief cognitive screening test in the pre-op screening clinic, such as the Mini-Cog, which just takes two to four minutes to administer. With the Mini-Cog, patients are asked to remember three words, draw the hands of a clock to show a specific time, draw the face of a clock, and repeat the three words they were asked to remember. The Mini-Cog can be an effective

way to assess baseline cognition. There's also several other brief cognitive assessment tools that are discussed in our paper that can be used as well.

DR. DEINER:

The third best practice recommendation for postoperative brain health involves intraoperative management. Can you tell us more about it?

DR. BERGER:

Sure. We recommend that anesthesiologists monitor age-adjusted end-tidal MAC fraction, that they strive to optimize cerebral perfusion, and that they use EEG-based intraoperative brain monitoring to titrate anesthetic management in older adults. Yet, more research is still needed to evaluate and compare specific brain function monitors, methods and approaches.

Our goal is to avoid relative hypotension, maintain normothermia, and reasonable anesthetic dosage. Uh, because some medications can contribute to perioperative neurocognitive disorders, or other forms of cognitive dysfunction outside of the perioperative care setting, the recommendations also advise anesthesiologists to consciously use or even avoid some of these medications in older patients. Thus, to promote post-operative brain health in older patients, anesthesiologists should avoid for example, using centrally acting anticholinergic drugs, benzodiazepines, Meperidine, and other drugs such as Diphenhydramine, Prochlorperazine, Haloperidol and Hydrocortisone because these drugs can contribute to the risk of confusion and inattention after surgery in older adults.

DR. DEINER:

And finally, the fourth recommendation for best practices for postoperative brain health concerns postoperative follow-up and management. What do you recommend?

DR. BERGER:

Well, it's clear that many of our older patients will experience perioperative neurocognitive disorders after intraoperative care, but there was little consensus in our group on who should follow these patients and manage these problems in the postoperative period. So, we recommend that more studies be done to evaluate the efficacy, feasibility and cost effectiveness of various follow-up strategies. We need studies to assess short and long-term cognitive outcomes after hospital discharge to study how to optimally manage these disorders, and to clarify who should follow these

patients after surgery and what patients should be told about the current understanding regarding recovery from these disorders in the longer-term.

DR. DEINER:

What role does the anesthesiologist play with regard to patient follow-up?

DR. BERGER:

So, outside of the pain clinic or intensive care unit settings, most anesthesiologists only see their postoperative patients a day or two after surgery for brief postoperative check. Because many cases of perioperative neurocognitive disorders don't become clinically apparent until after this point, if it all, most anesthesiologists likely will remain unaware of these cognitive issues in their patients. So we need more studies on how to optimize the post-operative care of these patients and how to best manage perioperative neurocognitive disorders.

We also need studies to evaluate the efficacy, feasibility and cost effectiveness of multiple strategies to assess outcomes, ranging from in-person clinic visits, to telephone calls and telemedicine, to automated electronic assessment tools ranging from apps to automated phone calls, to both physical and cognitive exercise programs, sleep hygiene, environmental and or drug treatment approaches. The bottom line is that a lot more work needs to be done. But the recent development of this standardized nomenclature using the umbrella term perioperative neurocognitive disorders and tools for perioperative outcome assessment can help us compare outcome measures across studies, institutions and even countries.

DR. DEINER:

Yes, and in the mean time there's a lot we can do to help improve the perioperative brain health available to older patients. With informed consent, cognitive testing or screening before surgery and standardized intraoperative management, we can help patients better understand their risk for perioperative neurocognitive disorders and we can allocate hospital resources to optimally care for high-risk patients to reduce the risk of delirium and improve recovery.

DR. BERGER:

Yes, absolutely. It's our hope that these best practices will serve as a starting point and as the basis for a more formalized evidence-based recommendation for minimizing the

impact of perioperative neurocognitive disorders and for optimizing postoperative brain health.

(MUSIC)

DR. STRIKER:

Brain health in older adults was also the subject of a recent conversation between Dr. Stacy Deiner and Dr. Michael Avidan, Professor of Anesthesiology at Washington University School of Medicine who discuss the ENGAGES Trial.

DR. MICHAEL AVIDAN:

The ENGAGES Trial, uh, randomized 1,232 patients who are 60 years and older and undergoing major surgery. One group received EEG guided anesthesia, and the other usual care group received what was typically usual care at our institution. And the purpose of the trial was to answer the important question of whether EEG guided anesthetic administration decreased the incidence of postoperative delirium in older adults undergoing major surgery.

DR. DEINER:

Michael can you tell us a little bit about how you came to study this question or what lead up to the study?

DR. AVIDAN:

Sure. Initially, I was doing research looking at EEG brain monitoring and intraoperative awareness. I actually led two large trials, one of which was sponsored by the ASA, looking into that problem.

Um, the research showed that with volatile anesthetic agents, setting an alert for a low volatile anesthetic concentration was as effective as EEG brain monitoring in preventing intraoperative awareness. But the question that arose out of that research, and it was very much debated in the field, was not only was it dangerous to get too little anesthesia but was there danger in giving too much? At the same time, there was a growing concern about perioperative brain health and postoperative delirium, which the ASA has embraced as a major focus.

So we wanted to address the question, could we as anesthesiologists, through what we do in the operating room, impact the likelihood that our patients will experience

postoperative delirium? Our research here at Washington University and at other institutions, showed that where there were patterns of EEG suppression, or flat lining of the EEG during surgery, there was a considerably increased risk of postoperative delirium.

Furthermore, and, and interestingly, that risk of delirium appeared to increase with longer durations of EEG suppression during surgery. So, really, the important question to answer coming out of this, was whether the suppressed pattern during surgery was causally linked to post operative delirium, or whether people with vulnerable brains were just more likely to have EEG suppression during surgery. And that was the impetus for the ENGAGES Trial in which we randomized older adults, as I described, having major surgery to have EEG guidance of anesthesia or to have usual care.

DR. DEINER:

Michael, the ENGAGES Trial found that postoperative delirium occurred in 26% of the EEG guided group and 23% of the usual care group, and that difference wasn't statistically significant. Were you surprised by the findings?

DR. AVIDAN:

Yeah, absolutely, Stacie. You know, contrary to our hypothesis, as you noted, there was actually an increase in delirium incidence by three percentage points in the EEG guided group. And, it's true that this increase was not statistically significant, but it was definitely surprising. And this is contrary to our hypothesis and really conflicted with results of previous studies that had examined this question. So, there have been at least three other trials, big trials, including one by our own group, that was a sub-study of the BAG-RECALL Trial, which was uh, one of the trials into intraoperative awareness and was funded by the ASA. And in all three of these large trials, there was the suggestion that EEG guidance of anesthesia could actually decrease postoperative delirium incidence. So now, you had the results of the ENGAGES Trial, which threw the cat among the pigeons in finding a result that really didn't seem to corroborate these previous studies.

DR. DEINER:

What clinical points would you take from your study findings?

DR. AVIDAN:

There was a lot that we learned, Stacie. So, first of all, it was really interesting and notable that we were able to teach anesthesia clinicians, including anesthesiologists, um, certified registered nurse anesthetists, residents, and student nurse anesthetists to recognize some of the key EEG patterns or features that are often seen during general anesthesia, in this case with a volatile anesthetic agent. Most importantly they were able to recognize EEG suppression, but there were also many other EEG features that they were able to recognize. It was also really notable that through the study, we showed that we could change practice in the real world, this was a pragmatic trial, and we showed that we could, uh, decrease volatile anesthetic administration by 14%, and there was almost a 50%, so half, decrease in the amount of time with EEG suppression in the intervention group.

Um, just something to comment on, because there's been so much interest generated by an exploratory finding, is that we looked at various other outcomes, but one intriguing post-hoc exploratory finding was that the 30-day mortality rate was lower in the EEG guided group than in the control group. So just to put that in context, only four patients died by 30 days in the EEG guided group, whereas 19 died by 30 days in the usual care group.

DR. DEINER:

That's a striking result. How does that compare with other studies?

DR. AVIDAN:

You know, that's a really important question, Stacie, because it's always necessary to ask is this a, a result that's plausible? And how does it fit with what we already know? And, and notably, I actually just did a meta-analysis on this, and most other studies that have randomized the EEG care or usual care have not found any impact on mortality. So, this result actually conflicts with what's already been published. It's a post-hoc exploratory finding so I think it should be reviewed as hypothesis generating and shouldn't over interpreted at this stage.

DR. DEINER:

And regarding your depth of anesthesia monitoring in EEG guidance during operating room cases, what do you think clinicians should take away from your study? Should they change their practice?

DR. AVIDAN:

Well, it's a difficult question. I certainly wouldn't jettison using EEG guidance, and you know, but we'll come back to that. Um, but at the same time I didn't think that you can say that EEG guidance can improve postoperative outcomes because the evidence frankly, is just too contradictory to draw firm conclusions. There are other large ongoing trials. So, in particular, I can think of two, there is the balanced anesthesia study, which is being conducted by colleagues from Australia and elsewhere around the world, which is randomizing over 6,000 patients to EEG guidance or to usual care. And their primary outcome is mortality at one year.

And, uh, we're actually conducting a follow-up partner trial to the ENGAGES trial called ENGAGES Canada and that's been funded by the Canadian Institute of Health Research. Uh, the principal investigator for this trial is Dr. Alain Deschamps in Montreal. Um, we're about halfway through enrolling to the study. It's also 1,200 patients, conducted at four Canadian sites, and importantly, it's focusing on patients undergoing cardiac surgery, which is a, a high-risk population. Similar to our previous ENGAGES Trial, the intervention is EEG guidance with the purpose of avoiding EEG suppression and this trial will also examine delirium as well as mortality as outcomes. So, I think certainly we'll have more information about both delirium and mortality following these trials, but I really want to caution that even after these trials are complete, it will be necessary to do a much larger pragmatic trial if we hope to answer these questions with more certainty and precision.

And the reason for this is that if there are differences, especially with mortality, but also with delirium, they're likely to be very small, and only a large study will provide precision to this question. And as I said the same applies to delirium, because I think we now know that if EEG guidance does prevent postoperative delirium, even in high-risk older adults, the effect is likely to be small. And, you know, all the trials that we've conducted are probably not large enough to detect small effects.

DR. DEINER:

So, Michael, given that your findings didn't show a, a difference in the incidence of delirium, should we be routinely monitoring the brain of adults during surgery?

DR. AVIDAN:

I'm glad you asked me that question, Stacie, because it's really a, a critically important question and one that's many anesthesiologists are asking. And in my opinion, absolutely, yes, we must monitor the brain during surgery. And EEG is a good way to do it. If you were to ask me can you provide hard data to show that it improves outcomes, my answer would be no. And I'm aware of that contradiction, but it's hard to show

outcome benefits with any monitor, Stacie, whether it's a pulse oximeter, an ECG a capnograph. I don't know that that matters. Monitoring the brain is really a good idea for our profession in principle because the brain is the target organ of general anesthesia. Why would we be monitoring every other vital organ and not the vital organ in which we are most interested? I think we should be doing everything that we can to monitor the brain. The EEG provides useful information during sleep and during anesthesia. And for me that is sufficient justification for monitoring. At the very least, the EEG provides information suggesting that traumatic awareness is unlikely.

DR. DEINER:

So, now what about eh, excessive depth? If you saw a, a patient having EEG suppression, should you go ahead and decrease anesthetic administration?

DR. AVIDAN:

Yes, so, obviously that's a question that follows from your last one and from ENGAGES, Stacie. And, as a point of principle, I think we should be targeting giving the appropriate amount of anesthetic for every patient under our care, and EEG suppression typically suggests that anesthetic administration might be in excess of what the patient requires. Um, it doesn't always mean that, but it often means that. So, although I can't say it will improve a patient's outcome, I do think I can say that you don't need to be administering general anesthesia to excess to achieve EEG suppression in the majority of instances. So when it does occur, I think that clinicians, that anesthesiologists and others in the anesthesia care team should decrease the concentration of anesthetic that they are administering.

You know, as I referred to earlier, there are important differences in EEG waves between people who are anesthetized and those who are awake, and the more you use the EEG during surgery, I think the more information you can glean from it, and the greater the benefit that you derive as a clinician.

(MUSIC)

DR. STRIKER:

Dr. Sharon Inouye, Director of the Aging Brain Center and Milton and Shirley Levy Family Chair and Professor of Medicine at Harvard Medical School. And Dr. Carol Peden, Professor of Anesthesiology and Executive Director of the Center for Health Systems Innovation at the University of Southern California talked about improving brain health after surgery, delirium and practical solutions.

DR. CAROL PEDEN:

What key things should anesthesiologists be thinking about in relation to your program and prevention of delirium?

DR. SHARON INOUE:

So I think with anesthesiologists, there are a number of areas that are exceedingly important. I think often anesthesiologists are involved in the preoperative screenings, and there can be, as you know, many preventive strategies put into place even prior to admission to make sure that patients are in as good shape as possible prior to the hospitalization. And so, educating patients about things to know before they come into the hospital, there are several educational pages and brochures that are on the same Hospital Elder Life Program website that are educational modules or packets of just like, what to know before you come to the hospital, what to bring to the hospital on the first day, you know, how to communicate with your physician, how your family can communicate with physicians and can advocate for you, what is delirium, you know, what are good things to do to prevent delirium? So, some basic things like that can be very helpful just to give a heads-up to patients about when they're there.

And then I think the other thing is to just make sure that everything is as optimized as possible in terms of, you know, metabolically in terms of, you know, activity, nutrition, the things that we know can help to build or maximize brain reserve. If they are on psychiatric medications, um, it's very good to think about how those will be managed during the course of the surgery. Sometimes, you know, patients are advised to taper off of things like sleep medications, or you know, anxiety medication. Sometimes they're not. It has to be very individualized, you know, alcohol use should be addressed, smoking should be addressed, glucose control should be addressed, you know, all these kinds of things, I think the anesthesiologist can be critical about in the preoperative setting.

During the perioperative period, obviously during the surgery itself, the anesthesiologist has a huge role in choosing which agents and which medications are going to be used preoperatively, intraoperatively, how monitoring will be done, you know, whether there will be this monitoring or not. And those are all areas where, you know, there are many studies as you know, Carol, to address how to optimize these approaches for older patients in the OR. And you're much more expert on that I'm sure than me, but one of the things as an internist that we do ask for and ask for our anesthesia colleagues when someone's at high risk, is to try to minimize anticholinergic medications for example, or to try to use more short acting agents where it's appropriate, and um, to use non-opioid

agents where it's appropriate. And so those are sometimes the conversations that we have as we're trying to optimize preoperative care.

DR. PEDEN:

Yes, and avoid benzodiazepines if possible. All those drugs on the Beers criteria which people can look at. Can I ask you, a little bit more perhaps about the pathophysiology and how is perioperative delirium related to dementia? And if you're an older patient and you get delirium, are you at greater risk for dementia?

DR. INOUYE:

Yes. Yes, so delirium and dementia are, are highly interrelated and dementia is the leading risk factor for delirium. So, someone who has mild cognitive impairment or unrecognized cognitive impairment is at very high risk for developing delirium. And then on the flip side, delirium is also a strong risk factor for subsequent dementia and work that we've done in our group, as well as others, have shown that, um, new onset dementia following delirium may be increased by as much as 12 fold increased risk, which is just huge and this is new incident dementia following a delirium.

I think the evidence is stacking that delirium may hasten cognitive decline both in those who don't have any cognitive decline to begin with, but there's also evidence that if people have already started on that pathway to decline, that delirium will accelerate it.

You asked, Carol, about the pathophysiology of that, and that is not really known. Um, there are a lot of hypotheses. There's a lot of exploration going on in that area. It seems that there may be inflammatory mechanisms that are contributing. There may be acceleration of neurodegenerative factors, things like apoptosis, um increased burden of amyloid for instance, maybe potentially triggered by operative or perioperative factors or by inflammatory cascades that are set off. So it's an area of very active investigation, and I think, I, I feel very excited that we may have some answers in the next, you know, upcoming years to what are the strongest pathophysiologic elements and, even more importantly, what can we do to intervene to prevent the decline.

DR. PEDEN:

I know you're right. It's such an exciting area of research. Now, you've shown that approximately 40% of cases of delirium may be preventable with some of the measures that we've talked about. But then 60% of cases may not be, so what would be the practical advice for anesthesiologists, um, who are managing those patients to help minimize the impact of that event?

DR. INOUYE:

Yes. This is a really important point that 60% may not be preventable totally. But we also have evidence that similar strategies to the Help program may be able to make the delirium less severe and of shorter duration. And, and that's really critical, and I think that to really treat delirium, you know to really eliminate it from occurring in that remaining 60% of patients, we are going to have to understand the pathophysiology and be able to approach patients with medications and other, you know, approaches. It might be cognitive reserve enhancement, or it might be anti-inflammatory medications or it might be sleep agents. Um, you know, I'm not sure. I, I think it's going to be a multifactorial approach.

But you were asking for practical advice about, um, how to implement these strategies, how to run a Help program. So, Carol, to get back to that question for practical advice our Help program including my team and other teams um, throughout the country in the world have looked at how you implement and sustain a Help program successfully long-term. And so just a few of the learning but I think might be helpful for your listeners are, it's very important to gain support from your hospital administration, you know, from the higher-ups in the organization and to have effective champions at the high-up levels. People that really know about the program, and who are very supportive and who realize how, you know, detrimental delirium is. And then the next challenge is to try to shift organizational culture to really embrace excellence in this area in providing better care for older patients and providing optimal perioperative care and preventing delirium in older adults, and I think that's happening at many hospitals.

(MUSIC)

DR. STRIKER:

Thanks for listening and thank you again to the Perioperative Brain Health Initiative supporters, Edwards Lifesciences, Massimo and Medtronic whose contribution help provide tools and resources to optimize the cognitive recovery and perioperative experience for adults 65 years and older. Join us for another episode of Central Line, coming your way soon.

(MUSIC)

VOICEOVER:

American Society of **Anesthesiologists**[®]

Visit asahq.org/brainhealthinitiative for additional resources, peer reviewed literature, toolkits and more. Subscribe to Central Line today, wherever you get your podcasts or visit asahq.org/podcasts for more.