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Anesthesia Technique & Cancer Recurrence: What Do We Need to Know?

Dr. Sands:
Preclinical data has previously suggested that anesthesia technique might impact the risk of recurrence for cancer related surgeries, but large clinical studies have provided us with some valuable insights. One of the clinicians guiding those research efforts is here to share his insights on today's program.

Welcome to *Project Oncology* on ReachMD. I'm Dr. Jacob Sands. And joining me to talk about general anesthesia and its impact on cancer recurrence and outcomes is Dr. Dan Sessler, Michael Cudahy Professor and Chair in the Department of Outcomes Research at the Cleveland Clinic.

Dr. Sessler, thank you for joining me today.

Dr. Sessler:
It's a pleasure.

Dr. Sands:
So let's begin with some background. Dr. Sessler, can you outline for us just the different types of anesthesia that are generally used at the time of cancer surgery?

Dr. Sessler:
Yes. I would say there are two broad types. One is general anesthesia, and the other is regional anesthesia, which could be neuraxial, such as spinal or epidural, or it could be peripheral nerve blocks. And then within general anesthesia, you could divide, into volatile anesthetics these are the gases like sevoflurane, desflurane, isoflurane, and then intravenous anesthesia, drugs like propofol.

Dr. Sands:
Now, we're going to get into some of your research, but there was some preclinical work that really led to your large studies, and I've come to learn that there is some preclinical work that suggested that maybe different types of anesthesia would have different impact on cancer recurrence. Are you able to outline that as the basis for some of the larger studies we're going to get to?

Dr. Sessler:
Absolutely. So there's considerable molecular, cellular and animal evidence that general anesthetics, especially volatile anesthetics, impair natural killer cell function. Natural killer cells, of course, are the primary host defense against cancer, and so they really matter, because people now believe at the time of diagnosis there are already circulating tumor cells all over the body. What prevents them from becoming metastases is natural killer cells. So, at the time of surgery, which is another reason why cancer cells may be distributed around the body, the last thing you want to do is impair natural killer cell functions. But general anesthesia and surgery do both. So, volatile anesthetics directly impair natural killer cell function. Opioids, which most patients get, also impair natural killer cell function. And finally, the stress response to surgery impairs natural killer cell function. So, basically, right at the time when patients really need good host defense against cancer we're doing three things to impair host defense.

Regional anesthesia might help though, and the reason is that regional anesthesia decreases or eliminates the need for volatile anesthetics, regional anesthesia is analgesic, so it decreases the need for opioids, and finally, regional anesthesia decreases at least some of the neuroendocrine inflammatory response to surgical tissue injury. So that was the basis for thinking that regional anesthesia might be beneficial, and animal studies did support that.

There were then many observational analyses, some by us, some by others, and some showed benefit, and some did not, and that

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included ours, some of which showed benefit and some of which didn't. So, observational analyses, retrospective studies, are always confounded. Nobody knows to what degree they're confounded, so they're exploratory. They shouldn't be considered a basis for treatment. But clearly, there was controversy here, and clearly, there were fundamental mechanisms, physiological basis for believing that regional anesthesia might be protective.

Dr. Sands:
These are very interesting concepts that led you to do multiple large studies to evaluate the validity of this preclinical work that you've discussed. Could you outline those results for our audience?

Dr. Sessler:
So that led us to do three major trials of regional anesthesia. The first of these was a 2,100-patient trial in breast cancer. So patients were randomized to a conventional general anesthetic with volatile anesthetics or to paravertebral blocks combined with propofol sedation. Patients were followed for many years afterwards, and there was absolutely no difference in cancer recurrence between the two groups. Thereafter, we did two others. One was an 1,800-patient trial in abdominal cancers, most of which were colorectal. So in this case patients were randomized to volatile anesthesia, general anesthesia, or to epidural anesthesia and sedation or as little volatile anesthesia as we would get away with. There was absolutely no difference in cancer recurrence, disease-free days alive or any other oncologic outcome in that trial. And then, finally, we did a 400-patient trial in patients with lung cancer who were randomized to conventional volatile general anesthesia or to epidural anesthesia and mostly propofol sedation. Once again, there was absolutely no difference in cancer recurrence or disease-free survival.

So, taken together, we have a very large number of patients here. Forty-five hundred patients or so have been entered into formal randomized trials of regional anesthesia versus general anesthesia, and there was no benefit, so I have to conclude, okay, it was a good idea; it was supported by basic science and animal science; but, as is so often the case, it simply doesn't translate to humans. From a clinical perspective, it's clear. You should not select the type of anesthesia based on expectations about cancer recurrence. If you want to use regional anesthesia, regional anesthesia is great. There are many other good reasons for using regional anesthesia, but cancer recurrence is not among them.

Dr. Sands:
For those just tuning in, you're listening to *Project Oncology* on ReachMD. I'm Dr. Jacob Sands, and I'm speaking with Dr. Dan Sessler about anesthesia use in cancer surgery and the potential implications for cancer recurrence.

Now, Dr. Sessler, you have outlined multiple studies that essentially demonstrated, no significant difference in recurrence related to the type of anesthesia use, which is somewhat reassuring, as I'm often telling patients that surgery is not going to impact their recurrence and this is kind of a fable out there, in general concerns about surgery, so it's reassuring to hear that the anesthesia type is not necessarily something that's going to impact that. But that being said, there is still a lot to look at in the field going forward, and so, are you able to highlight some of what you're looking at now in ongoing studies?

Dr. Sessler:
Absolutely. So I mentioned in the beginning that there are two types of general anesthesia: volatile anesthesia and intravenous anesthesia. Preclinical data again suggests that intravenous anesthesia is preferable to volatile anesthetics.

There's basic science evidence that volatile anesthetics impair natural killer cell function, and intravenous anesthetics, particularly propofol, which is the major intravenous anesthetic, either leave natural killer cell function unchanged or maybe even slightly improve it. So, based on these data, we have the theory that total intravenous anesthesia might be preferable to volatile anesthesia in terms of cancer recurrence.

There are also other anesthetic adjuvants. For instance, Cox-2 inhibitors might be helpful. Lidocaine, intravenous lidocaine, might be helpful. And again, there's basic science evidence to suggest that this might be helpful, but as we well appreciate, lots of things that are true in animals simply don't translate to humans. So we will have trials eventually testing all of these things, and we'll see. If we're lucky, something we do in the perioperative period, something related to anesthesia, might actually reduce cancer recurrence. Given that cancer is the second leading cause of death worldwide, that would be a huge advance. Even the tiniest reduction in cancer recurrence would be a really big deal.

Dr. Sands:
Now, you've covered a lot of ground as far as these perioperative, anesthesia methods. Is there any takeaway for clinicians to particularly discuss with patients around their choice of anesthesia at the time of surgery?

Dr. Sessler:
Absolutely. So our results are clear. Regional anesthesia is not protective against cancer recurrence, but this is an important result

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because some patients want regional anesthesia because it does, in fact, provide good analgesia. Generally, anesthesiologists recommend regional anesthesia because it actually is really helpful, but other patients don't want a needle in the back or something similar, so patients have strong preferences for one type of anesthesia or another. What these results show is that we can respect patient preference here and it will not impair their care, so patients should not be told, "You should get a paravertebral block because it will reduce your risk of cancer." That's not true. If patients want one, they can have one, or if they prefer general anesthesia alone, that's perfectly acceptable also, and their long-term cancer risk will be identical with either one. So, this is an area where we can absolutely give patients autonomy.

Dr. Sands:
And with that recommendation, it wraps up our time. I want to thank my guest, Dr. Sessler, for joining me today and sharing his expertise on the use of anesthesia and cancer surgery. Dr. Sessler, wonderful having you on the program.

Dr. Sessler:
It's my pleasure.

Dr. Sands:
I'm Dr. Jacob Sands. To access this and other episodes in our series, visit reachmd.com/projectoncology, where you can Be Part of the Knowledge. Thanks for listening.

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