Dr. James Rathmell: Hello. I’m Jim Rathmell, Professor of Anesthesia at Harvard Medical School and one of the executive editors for Anesthesiology, and you’re listening to an Anesthesiology podcast designed for physicians and scientists interested in the research that appears in the journal.

Today, we’re going to talk with the authors of a publication that appears in the September 2016 issue. Helping me with today’s interview on behalf of the journal is BobbieJean Sweitzer, Professor of Anesthesiology at Northwestern University and an associate editor for Anesthesiology. Dr. Sweitzer, thanks for joining me.

Dr. BobbieJean Sweitzer: Thank you, Dr. Rathmell. I’m delighted to be here, especially having an opportunity to speak with Dr. Roth, who is a former colleague of mine at the University of Chicago.

Dr. James Rathmell: With us today are two senior statesmen in the field of anesthesiology. Dr. Steven Roth, who is Professor Emeritus in the Department of Anesthesia and Critical Care at the University of Chicago, and now the Michael Reese Endowed Professor of Anesthesiology, and Professor of Ophthalmology at the University of Illinois College of Medicine in Chicago, Illinois. Dr. Roth is the senior author of an article titled, “Perioperative Visual Loss in Spine Fusion Surgery: Ischemic Optic Neuropathy in the United States from 1998 to 2012 in the Nationwide Inpatient Sample.” Welcome, Dr. Roth.

Dr. James Rathmell: Thank you, Dr. Rothmell.

Dr. James Rathmell: Joining Dr. Roth is Dr. Michael Todd, who authored an accompanying editorial titled, “Good News: But Why Is the Incidence of Postoperative Ischemic Optic Neuropathy Falling?” Dr. Todd is Professor Emeritus of Anesthesia at the University of Iowa Carver College of Medicine, Iowa City, Iowa, and now Professor of Anesthesia at the University of Minnesota in Minneapolis, Minnesota. Dr. Todd, thanks for joining us.

Dr. Michael Todd: It’s a pleasure. Thank you, Jim.

Dr. James Rathmell: Dr. Roth, congratulations on the publication of your work. Emerging from anesthesia with blindness has to be among the most frightening complications that any patient can contemplate, associated with surgery. A number of previous investigators have found risk factors that are associated. Can you tell us how this study was done and how you set out to teach us more, or help us to learn more, about ischemic optic neuropathy?

Dr. Steven Roth: The way that this study was done that differed from the previous studies, is that we tried to get a very large sample of patients who underwent spine surgery, that would be representative of a national sample of patients who were subjected to the surgery. The reason why we need to do that is because this is a very rare complication, and the previous studies up until this time had either consisted largely of case reports, small case series – and the largest one that I think you referred to, I was a part of in 2012, in which we had about 80 patients with ischemic optic neuropathy, who underwent spine fusion, and controls were selected from a group of 17 institutions.

Now, that was a very informative study. But the point here was to gather a much larger sample, with the goal that, by having a larger sample, we would be able to have a greater power to make conclusions about risk factors, particularly those that existed preoperatively, so that we might be able to better predict who is at high risk for this complication; and in turn, that might alter the process by which we give informed consent to patients, and perhaps even the surgical planning for the procedure.

Dr. James Rathmell: Tell us more about this Nationwide Inpatient Sample. Is it really representative of the patients that readers of Anesthesiology might be caring for in their everyday practices?

Dr. Steven Roth: In my view, it is representative. The way the sample is derived is that, in every hospital, there’s a series of discharge, procedure and diagnostic codes that are catalogued. So, the way this database works is that those codes are taken from, as it turns out, a sample of approximately – at first, I should say, up until 2011, it was taken from a random sampling of 20% of US non-federal hospitals. All it has in it are those discharge codes. You cannot identify an individual patient or subject using this database.

Now, in 2011, the database changed so that, now, it samples the entire United States hospital population, again with the exception of the non-federal—for example, the VA system. Therefore, what you have here are discharge records from practically every type of hospital in the United States. And therefore, I think it’s very reasonable to say that this is representative of what readers in the United States would encounter in their daily practice in the hospital.

Dr. James Rathmell: And that was just about 2½, or just over 2½ million, of these spinal fusion surgeries. Is that right?

Dr. Steven Roth: Right. And that appears in table four in the paper, and it’s just about 2.5 million. It needs to be clarified that what this represents is known as a national estimate. Bearing in mind that this is a sample of the United States hospital population, there then has to follow some math in which is derived the estimates for the nation. So, this number should not be taken literally. Nonetheless, that is the national estimate. And 2½ million patients is clearly a very significant sample.

Dr. James Rathmell: And that’s the point, is that’s a pretty big sample size. So, you and your co-investigators identified four factors associated with visual loss: increasing age; male sex; blood transfusion; and obesity. Can you postulate why these conditions may cause this devastating injury?

Dr. Steven Roth: The two that I’ll start with first would be obesity and transfusion. It was shown previously, in our 2012 study published in Anesthesiology, which was the case control study of the 80 patients with ischemic optic neuropathy in spine surgery, that one of the things that conferred higher risk was obesity. It was postulated at that time— and I still would hold by the same postulate—that the patients who are obese – when they’re placed in the prone position, there are issues such as increased venous pressure and perhaps increased airways resistance, which would increase the venous pressure going into the head. According to this theory, the increased venous pressure in the head would be causing either a true venous infarct, to take it all the way to the pathophysiology, and/or it would be producing simply effect of increased venous pressure, and in turn decreased delivery of blood and oxygen.

Now, that which I just said remains very speculative. Because, to date, there have not been any studies that have measured any of those
parameters. There have been studies that have measured intraocular pressure. However, that does not reflect the venous pressure that is coming from the draining veins in the optic nerve.

The second factor which I’m going to discuss is transfusion. Again, in the 2012 study, relatively high blood loss was one of the risk factors. Here, in this case, we take it that transfusion is a surrogate for either lots of blood loss and/or long surgery with lots of fluid. But that is as far as we can take it at this point.

With respect to age, we don’t know exactly why increasing age confers a higher risk. This is, however, a new finding compared to previous studies. Among the possible reasons for this would be either that older people undergo more complex operations, longer operations, and/or they have certain medical risk factors that go along. However, the third factor, at least with respect to the medical risk factors that we looked at, was not co-linear. Meaning, it did not automatically accompany the increased age. So, we were able to isolate out age for itself. So, whatever we can say about age, therefore, remains still somewhat speculative.

One of the most interesting findings is that it’s good to be a woman if you undergo this procedure. What’s known as the incidence risk ratio—the IRR—was 0.3 for women compared to men. This means that a woman has about only one-third the chance of developing this complication compared to a man.

We don’t know why this is. One possible reason for this would be because of the effect of estrogen. It is well-known that postmenopausal women are more prone to stroke and its complications compared to premenopausal. And that, in many studies, has been looked at and is believed to be due to estrogens. However, in a sub-analysis of the work, there was no influence of age in women on this risk ratio. So, therefore, at this point, it remains unclear exactly why women have an advantage compared to men.

**Dr. BobbieJean Sweitzer:** Dr. Roth, in this study you reported on visual loss related to ischemic optic neuropathy. However, there are other etiologies of perioperative visual loss. Can you help us understand the differences in the underlying etiologies of blindness associated with surgery, specifically the pathologic differences among ischemic optic neuropathy, retinal arterial occlusion, and cortical blindness? Are the prognoses different?

**Dr. Steven Roth:** Yes. The most important and most common cause of visual loss in this setting of spine fusion is in fact ischemic optic neuropathy. And the cause of that is traced to the optic nerve, either the anterior portion of the optic nerve, in which case it’s called anterior ischemic optic neuropathy, or posterior, which means it’s behind the eyeball, and it’s called posterior ischemic optic neuropathy.

To this day, it still remains unclear exactly how someone gets ischemic optic neuropathy. The pathophysiology is still not totally understood and still needs some work. But it has been speculated—and not only speculated, I should say, but also, based upon our study and based upon others—that it appears to be several factors which either come together or exist by themselves, and include things like blood loss; lengthy surgery; obesity; positioning on a Wilson frame; being a man; being obese; and being older. Again, it’s not for now to talk about precisely how all of that comes together, because we really still don’t know the whole story.

But retinal artery occlusion, as opposed to affecting the optic nerve, affects the retina. The retina is the sheet of nerve cells through which the signals — after the light strikes the photoreceptors in the back of the eye, the signals are transmitted through several layers of retinal nerve cells, and then finally sent on to the brain via the optic nerve. And the retinal artery occlusion is a specific entity where either clot, air, or other material, either through a spontaneous occurring thrombosis, or through an embolism, or other rarer causes, causes an obstruction—either a complete or a partial obstruction—either of the central retinal artery or a branch retinal artery.

And this entity — unlike ischemic optic neuropathy, where it’s not possible to see the lesion by a routine ophthalmological examination if it is behind the optic disk, meaning posterior ischemic optic neuropathy, the examination in that case remains normal. There are specific signs and symptoms, and specific findings on the ophthalmological examination, the fundoscopic examination — such as pallor of the retina; what’s known as the cherry-red spot, which does not always appear—which allows the diagnosis to be made readily.

The third entity is called cortical blindness. Cortical blindness is an effect upon the occipital cortex, and that is oftentimes in the context of stroke. These three entities can be distinguished mostly by ophthalmological diagnosis, and sometimes supplemented with things like MR and CT. And there is a table in the current edition of Miller in my chapter on postop visual loss, that shows the diagnostic steps and how you differentiate between these three.

**Dr. BobbieJean Sweitzer:** So, you’ve noted that women are much less at risk for visual loss in the perioperative period. Can you enlighten our audience on some of the other characteristics that you examined that you found were not associated with visual loss? And were there any in particular that surprised you, and why?

**Dr. Steven Roth:** Among the things that were not different included hypertension, diabetes, peripheral vascular disease, atherosclerosis, coronary disease, smoking, and carotid artery stenosis. People who have vascular disease or vascular risk factors would be at higher risk for this disease. And this was not the case in this very large study.

One factor that looked like it actually was going to be significantly different between the affected and the unaffected was stroke, because stroke had an incidence risk ratio which is, in this case, for — you could think of it pretty much the same way you think of an odds ratio, because this entity is so rare. And that was seven times as high in those who were affected versus those who weren’t. But when we ran the statistics, there was such a wide variation in this, that it was not quite to the level of where we would say that it was statistically significant. So, it was a trend, and this requires further study to determine if stroke is a risk factor.

However, that said, one of the things that we really cannot determine is whether or not the stroke was something that the patient had coming into this hospitalization, and therefore we would say that it could be a true risk factor; or whether it was something that developed during the hospitalization, perhaps at the same time. Or, it could be it was diagnosed as a stroke and written down on the diagnosis list as a stroke, but in the final analysis it really was not a stroke.

This points out one of the downsides of this type of analysis, which is that we don’t have a way to confirm the diagnostic codes in any of the cases. And there’s always the possibility of overdiagnosis or underdiagnosis. That might explain why the stroke appeared to be seven times a higher risk; but in the end, it really was not significant.

**Dr. James Rathmell:** Dr. Todd, the good news from this new analysis is that the incidence of postoperative ischemic optic neuropathy appears to be decreasing. Do you think that’s due to the conscious efforts of anesthesiologists and surgeons to prevent this complication, or is it an unintended consequence changes in either our patients or maybe the conduct of anesthesia and surgery in general?

**Dr. Michael Todd:** That, of course, is the great unknown. I think the reality is that it’s probably a little bit of both. Certainly, starting back in the early phases of, sort of, the late 1990s or early 2000, when we saw tremendous increase and interest in this problem, I think because of the increasing number of spine surgical procedures and the number of cases that were being reported, people started talking about it. The American Society of Anesthesiologists got involved in producing some advisories. This was material that was beginning to appear, both in the orthopedics and in the neurosurgery literature. So, there was obviously a big increase in awareness of the problem.
The difficulty with attributing the improvement to an intentional change in practice is that the data on the risk factors is much more recent than that. Like Steve, I was part of the 2012 case control study, which really was the first objective piece of information to identify risk factors for the disease. And if you don’t know what the risk factors are, how do you knowingly change your practice to improve something? And the incidence of this problem was falling, based on Steve’s recent paper. The incidence of this problem was dropping before this information came out. So, it can’t entirely be due to intentional changes in practice.

My personal feeling is that – and this is mostly the content of the editorial, is that most of the risk factors are not under our control, and in fact are probably worse over this timeframe. Patients are older; they’re more likely to be fat; there’s no change in the gender mix, and so on and so forth. Of course, those are things we can’t control anyway. So, my guess is that a big portion of this is changes in practice that were taking place independently of our knowledge of the problem, but which coincidentally led to an improvement or a reduction in the incidence of visual loss.

Dr. James Rathmell: In a previous study, the use of the Wilson frame was associated with this loss of vision. Can you explain what a Wilson frame is, and why it might be associated with a higher incidence of blindness?

Dr. Michael Todd: Yes. I suspect that most anesthesiologists are familiar with the Wilson frame, because it was so widely used in years past. Perhaps some of the younger anesthesiologists haven’t seen it. But this is a – I guess it’s a mechanical chest roll. It’s two longitudinal pads that are arched. There’s actually a spring device that will allow you to change the height of the arch. And the patient is draped over that frame. It creates a bit of a curvature in the back, so it makes it easier for the surgeon to access, for example, intervertebral disks.

The problem with it is that the abdomen does not hang freely, and there’s actually pressure on the abdomen; therefore, I – we think, increasing venous pressures. Actually, we – there is published data suggesting that venous pressures are higher in people positioned prone on a Wilson frame. Obviously, the larger someone’s abdomen is – i.e., someone who’s obese – the more pressure is applied to the abdomen.

And that’s one of the reasons that we came to believe in the potential role for elevated venous pressures in this disorder. There isn’t any data that I can find in the published literature, talking about different prone positioning devices.

So, I did a little survey of my colleagues in the neurosurgical community. And basically, unanimously, they commented that the Wilson frame has largely disappeared from surgical practice for long spine procedures; still used for short, single-level lumbar laminectomies, but that’s not a particular risk for vision loss. And I postulate – although, again, with only limited information – that it’s the disappearance of the Wilson frame which is the single biggest risk factor we could identify. It’s the disappearance of the use of the Wilson frame that may be playing a role in this change.

Dr. BobbieJean Sweitzer: Dr. Roth, you’ve also done some basic science research to better understand both the physiology of the eye and visual loss. Can you elaborate on what you have found in those studies, and how it may help us understand the association of the characteristics you identified in this current study and perioperative visual loss?

Dr. Steven Roth: Firstly, we have to divide this up into the studies on the retinal side and the studies on the optic nerve side. On the retinal side, over the years, we’ve learned a tremendous amount about the natural history of retinal artery occlusion. Which, again, is not the main cause of this problem; but it’s important to mention, because one of the easy things to avoid in a patient who’s positioned prone for spine surgery is compression on the eye.

Now, as it happens, if the eye is compressed, even for a brief period of time — and this is in animal studies — even for 15 minutes, that is enough to produce damage. And this is one of the reasons why it’s very, very important to check and to document when the patient is positioned prone, regardless of what kind of headrest you have, that the eyes are free of pressure. However, pressure on the eyes is not the cause of ischemic optic neuropathy.

Now, we tried to produce ischemic optic neuropathy in a rodent model. And the way that we did that was by placing them in an extreme head-down tilt and by hemodiluting them. And under those circumstances, a functional parameter that — based upon certain light flashes, that measures the nerve impulses as they go into the optic nerve, was significantly affected by those two things: putting them in the steep head-down tilt, and hemodiluting them; as well as some other changes that could be seen under the microscope.

These data are not yet published, but they do suggest that we can, at least to some degree, reproduce some aspect of this injury in an animal model. And once we’re able to do that, then we could begin to look at what types of things could be done. Could anything be done intraoperatively, either to monitor the patients – for example, is there some type of simple, or maybe not necessarily simple, but is there some type of test that can be done to examine those who are at risk as it’s happening? And then, of course, beyond that, the possibility of either some specific intervention; or even doing something that would be benign, that could be given to the patients beforehand to hopefully completely eliminate the risk.

Dr. James Rathmell: Dr. Roth, you’ve already told us in this Nationwide Inpatient Sample that it doesn’t have any of the intraoperative data like anesthetic technique or the length of surgery; even surgical positioning; blood loss. Can you envision a way, or have you embarked on any further studies, to try and get at those factors more directly?

Dr. Steven Roth: So, that is, of course, one of the disadvantages from the point of view of looking at perioperative events: you’re not able to look at what happens during the anesthesia, and you have fairly limited coverage of what goes on in the postoperative period as well. As a result of that, we have actually done studies which are not yet published, in other databases, in which there is more perioperative information available. However, all of these have their drawbacks, including there are still certain pieces of information that cannot be extracted. It’s also smaller in terms of the number of subjects. And there are other disadvantages as well.

However, one of the things that we’re working on is that there are databases that do provide more of a longitudinal slice through the patient. Unlike this one, which is the NIS, where you only get a snapshot of information from one hospitalization, being able to analyze data in which you can distinguish between what factors were present preoperatively versus what developed during the hospitalization, and the follow-up to determine the accuracy of the diagnosis, would be very valuable. And that is going to be one of the next steps that we actually are taking now.

Dr. James Rathmell: Terrific. I hope today’s discussion will interest many of you who are listening today, and lead you to read this important article about perioperative visual loss to learn more. I want to thank doctors Roth and Todd for discussing their work with us today, and I wish you well as you continue your efforts to learn more about how and why perioperative visual loss occurs, and how we might eliminate the occurrence of this terrible complication altogether. Dr. Sweitzer, thank you, too, for joining today’s discussion.

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