NIREN ANGLE: Good afternoon. Thank you for having me in this lecture. I'm going to speak to you about abdominal aortic aneurysms, and I don't know if you want them to intercede with questions during the talk? I don't care either way.

SPEAKER 2: It's up to you.

NIREN ANGLE: OK, so if you have any pressing questions, feel free to just interrupt me, and I can answer them as needed. The idea of this lecture is to give you an overview of what has been happening in terms of the treatment of abdominal aortic aneurysms over the last 15 years or so. The question first becomes, well, how do you define an aortic aneurysm?

And an aortic aneurysm, or any aneurysm, is really a ballooning out of a blood vessel. So the normal diameter, which in the human aorta is about 1.5 to 2 centimeters, depending on whether it's a man or a woman, increases. And some people would consider 3 centimeters to be the definition of an aortic aneurysm, and others would use the diameter being 1.5 times the normal arterial size as a definition. It can occur in virtually any artery in the body, but as far as the aorta is concerned, 90% to 95% of those occur below the renal arteries in an infrarenal position in the abdomen.

And this just shows the anatomy of the aorta. This is the retroperitoneum, and here's the vena cava. Here is the aorta.

These are the renal arteries. This is the renal vein. This is the superior mesenteric artery. And as I said, 95% of the aneurysms occur below the level of the renal artery. And it can include, and frequently does include, the iliac arteries on either side.

The history of aortic aneurysms is quite interesting. In 1923, Rudolph Matas performed the first operation where he tied off the aorta. And as one can expect, the patient didn't do too well. His aneurysm didn't rupture, but other things did go bad.

There have also been attempts to use wires inside the aneurysm sac to induce thrombosis and this is a forerunner of what we use in interventional techniques today for other things where we put in coils. And the coils are basically these circle wires that cause a turbulent flow to occur, and then the clot forms because the flow is turbulent. So this was recognized way back in the 20s.

Rea first popularized trying to fibrose the aneurysm by wrapping cellophane around the neck of the aneurysm, and that actually worked to a certain degree. And Albert Einstein actually was offered by Michael DeBakey, if you believe him, or believed him. Michael DeBakey offered to fix the aneurysm for him by resecting it, but he declined. And he underwent the treatment of the cellophane, where they wrapped it.

And we don't know exactly what the site of the aneurysm was in Dr. Einstein. And he survived for five years, and then ultimately died from a ruptured aneurysm. The first resection was actually done in 1951 by Dr. Dubost.

It remains the 10th leading cause of death in men, particularly as you get older, and there are 8,500 hospital deaths in the United States. 30% to 50% of people die before they reach a hospital if the aneurysm ruptures, and after they reach the hospital, another 30% to 40% of those patients die. So if one can fix them electively, the odds are much better than if you wait for a rupture.

So the overall mortality-- the 80% to 90% that I've listed here is the most dire of statistics. The mortality from a ruptured aneurysm ranges from 50% up to 90%, depending on the particular circumstances, of whether it's a free rupture, contained rupture, how quickly they got to the hospital, et cetera. Elective repair of an aortic aneurysm has a mortality, but it's only anywhere from 1% to 4%, depending on where it's done, how it's done, et cetera. So the odds of dying from a rupture are vastly, vastly higher than an elective repair.

It's interesting, because more than 50% of ruptured aneurysms were palpable but were not detected or noted during a recent medical examination. And this was a study out of Australia where they looked at patients that had presented to the hospital with ruptured aneurysms. And when they went back and looked at the medical record for a year, those patients had been seen by a primary care physician. And the aneurysm had either been missed or not noticed, pointing out the fact that they're hard to find unless they're really big.

So the prevalence of aneurysms is about 4.5% in men and 1% in women. This is data from SAVE screenings. And so there are about 1 million people living in the United States with aortic aneurysms. They're not all of a size that needs to be treated, but it is still underdiagnosed.

So the question is that once you identify somebody with an aortic aneurysm, can you predict rupture? And the answer is not very well. There are four issues that I've outlined.

There are the demographic features-- are you male, are you female? Do you smoke? Anatomic features-- how big is the aneurysm?

Biologic features-- this is something we understand in the lab, in an animal study, but not in the clinical realm, in the sense of what's happening in the aneurysm wall that causes it to grow and then ultimately causes it to rupture? And then the question then is, how solid is our understanding of each of these components? And the answer is not very good. Even in this day and age, we don't understand this very well.

So I like Rumsfeld's Rules for a lot of things, but especially this one. There are known knowns-- there are things we know that we know. There are known unkowns-- that is to say, there are things that we know that we don't know. But the bigger question is there are unknown unknowns. There are things we don't even know that we don't know.

And with aneurysms, I think, that's the problem, is that we have those three things-- diameter, rate of expansion, and gender. That's what we know. And then the biological stuff is fuzzy in terms of animal models, because we don't have a good animal model of aneurysms that develops spontaneously. We can induce aneurysms by infusing [AUDIO OUT], and doing all kinds of other things, but that is an artificial way of creating an aneurysm, and it's not really the same as a human. So really, all we go by is essentially the size.

And this is from natural history studies going back to the 40s and 50s and 60s that roughly can be summed up as the following-- as the aneurysm size increases, the risk of rupture increases. So if your aneurysm is small, i.e. 4 to 5.5 centimeters, your risk of rupture annually is probably about 1% to 2% per year. Quite small.

Then you get up to-- and these are artificial stratifications-- but if you go 5.5 to 5.9, you're risking about 10% per year. 6 to 6.9, 10% per year. If you go up above 7, it goes up. So if I see somebody with an 8 or 9-centimeter aneurysm, you can safely say there's about a 30% annual risk of rupture, meaning that over the next three years, you're virtually guaranteed you're going to rupture.

So the bigger they are, the more urgent that it is necessary to be treated. So if somebody comes into the emergency department or into your office with a 10-centimeter aneurysm, that person should be fixed in the next week or two. If somebody has a 5-centimeter aneurysm, that person probably should be fixed, but you can fix them a month later, two months later, three months later, and so on.

This is a study that looked at-- and this was a study called the ADAM study, the Asymptomatic Detection and Management of Aortic Aneurysms, published in JAMA, came out of the VA. And that essentially showed the same thing. Now, if you look, these are the years of study that they were followed and in proportion with rupture.

And this is the 7-centimeter cohort, this is the 6, 5.9-centimeter cohort. Now, for the first two years or so, there's a big difference in rupture rate. And then after the first two years, they both start climbing, and at some point about four to five years, the curves start crossing. So that tells you that those other patients had their aneurysms continue to grow.

And this was another study that looked at-- a randomized controlled study looking at aortic aneurysms and randomizing small aneurysms defined as 4 to 5.5 centimeters to management by observation or immediate operation. And the takeaway that some people took away, which some like me would dispute-- if you look at the survival curve, they're virtually identical, the surveilling group and the need to repair group. Meaning that if you've got a patient with a 4 to 5.5-centimeter aneurysm, you can watch them. And when they grow, then you can treat them. There is no additional risk to observation.

It was actually 5, 5.5, not 4. But if you look at this, repair of abdominal aortic aneuryms in the need to repair group-- 93% were operated on. But in the observation group, 62% were operated on.

And the reason for that-- and this is where some people would take exception to the conclusions that the authors reached-- yes, it is safe to watch them, because you can operate on them if their aneurysm starts to grow. But the majority of these patients will have their aneurysm size increase. So you're going to end up fixing the majority of them.

And so this then has to be looked at in the context of the population that you're treating. If they are reliable, and they can get surveillance, ultrasound, or CTs on a regular basis, where you can keep an eye on them, this may be a good strategy. But for those like-- I've been at hospitals and universities where you don't have reliable patient follow-up. And those patients, if you have a 5-centimeter aneurysm, and you tell them, "Come back in six months, we're going to do an ultrasound," the great majority of them never did. So in those patients, if you don't do this, you might lose them, and they will rupture and potentially die.

So aneurysms grow, and they grow in a very irregular pattern. It's a staccato pattern. So you

may have an aneurysm that stays at same size for six months, a year, and then suddenly grows, and then stays the same time for another six months to a year, or two years, or three years. So it is critical that they be surveyed at least every year and probably every six months once they reach a certain size, if you're not going to operate on them.

So of that, so this was the UK equivalent of the American study, VA study, which was called the UK Small Aneurysm Trial. And that shows essentially the same thing. 4 to 5.5-centimeter aneurysms, ultrasound surveillance versus early surgery-- and this is just people undergoing surgery.

And not surprising, people who were randomized to the surgical arm have surgery, so they're up here. The surveillance arm-- they're down here. But if you watch two, three, four, five years, most of them start going to this point, where they all end up having surgery.

So once again, maybe with the National Health Service, this might be strategic to do this, where you can say, well, we don't need to do anything until you reach 5.5 centimeters if you have a captive population. But if you don't, then most of us, if you reach 5 centimeters, we will repair the aneurysm. We don't wait until 5.5. And in women, 4.5, because size for size, women have a higher risk of rupture. And indexed to the woman's body size, a 5-centimeter aneurysm in a man is comparable to a 4.5-centimeter aneurysm in a woman.

The mortality rate-- this would be considered an outlier in this day and age. 5.8% in surgery and 7.1% in surveillance. I mean, in Centers of Excellence, for those of us who do this all the time, the mortality rate from elective aneurysm repair should be about 2% to 3% at most, not 5.8% to 7%.

The interesting data that came out of that also was that the median aneurysm growth rate was about 0.3 centimeters per year. And so there are two things that we use in terms of following a patient. If their aneurysm is of a certain size, i.e. 5 centimeters or greater, we will repair. Or if the growth rate exceeds 0.5 centimeter per year, even if they don't reach 5 centimeters, we would repair.

So those are the two things that we look at. So their conclusion was ultrasound graphic surveillance for small aortic aneurysms is safe, and early surgery does not provide the long-term survival advantage. And they did not support a policy of open repair for aortic aneurysms of 4 to 5.5.

So does size matter? In this case, yes it does. Natural history data shows that the larger the aneurysm, the higher the risk of rupture.

And then this is what I was talking about before. Does a policy of surveillance makes sense in all populations? So it's just like most prospective randomized trials-- it's not real-world data. It's very highly controlled, very highly followed up. And you have to always look at that in the context of the population that you're trating.

All aneurysms will grow. Aneurysms don't stay stable. It's just a matter of time, and we don't know the timeframe. As I said, they grow rather erratically. And then those are the sort of factors that we use in terms of managing patients and deciding when to intervene on them.

So these are the known unknowns. We know that we don't know this. Rate of expansion and risk of rupture-- we assume if it's more than 0.5 centimeters every year, then that is a high risk of rupture. Never been really proven, but that's sort of a takeaway.

Gender-- we do know that a female with aortic aneurysms-- so it's about a 7-1 ratio in aneurysm incidents, male to female. So it's unusual to have it in a woman. But if you do have it, if a woman does have it, she's at higher risk of rupture for a given size for the same size aneurysm in a man.

Biomechanical forces-- I might have a couple of slides to show you where you can do finite element analysis, which is a computer modeling of the sheer stress and forces on the aneurysm wall, and then correlating it with where the rupture is to see if we can define any better what are the features that cause an aneurysm to rupture, no matter what the size. And then the role of enzymes in aortic aneurysm. The enzymes are elastase, and what has been shown is that there is a circulating level of elastase that is present in patients with aortic aneurysms. And whether the aorta itself is the inciting event or the source of the elastase is not clearly known, but there is a humoral factor that causes, in addition to hypertension, aneurysm walls to degenerate.

So once again, unoperated AAA-- if your aneurysm is less than 4 centimeters, the growth rate is about 0.5 centimeter per year, and 4 to 4.9 is about 7 centimeters per year-- I'm sorry, 6.9 millimeters. And then more than 5 centimeters it's 7.4 millimeters then. Yes?

SPEAKER 3: Is the ultrasound accurate [INAUDIBLE]?

NIREN ANGLE: Excuse me, it is. There is about 0.5%-- I'm sorry-- question. Thanks, Bob.

Question is, is ultrasound accurate in measuring size of the aneurysm? And the answer is yes. Now, ultrasound is a very operator-dependent test. So if the ultrasound technologist in the lab is reliable, and it's a validated lab, then yes.

But when I was at UCSD or UCLA, we used to get patients from all over the place with ultrasounds done elsewhere. And we would repeat them, and the 90% stenosis for a carotid was a 40%, and vice versa. Aortic aneurysms were the same way, so it is very operator-dependent.

SPEAKER 3: [INAUDIBLE].

NIREN ANGLE: Right.

SPEAKER 3: [INAUDIBLE] . --here and there, making such a big diffeence, I always wondered, whe I'm looking at this data, how do I trust it, and support it.

NIREN ANGLE: That's absolutely correct. So if you get something from outside that you don't know the validity of repeated, or if you can get a non-contract CT, so if you're just looking for the size. Because you can tell the diameter just on a non-con CT so you don't expose them to the contract.

There's a 0.5 centimeter or so error rate in the literature between ultrasound and CT. And it's not whether it's higher or lower. It just seems to be about 0.5 centimeter off, which can make a difference.

So if I see somebody with a 4.9 or a 5.2, I will get a CT. I'll probably fix it, because a 0.1 centimeter distinction is rather esoteric and fetishistic. It's not really clinically relevant.

So if it's a 4.5, I will get a CT, because the other thing that you miss on an ultrasound, depending, once again, on the technologist, is you miss the iliac aneurysms. You miss the internal iliac artery aneurysms.

So if somebody comes to me, I always get a baseline CT scan-- that way I know the entire anatomy. And then I can choose to follow them with ultrasound, because I know where I start. So that's usually my strategy.

So the natural history of an abdominal aortic aneurysm is to expand and rupture. This CT scan just shows an aneurysm that has ruptured and has filled, at least temporarily-- you can see the little [INAUDIBLE] in here, and this is all a hematoma.

And remember that the aorta has a retroperitineum that is of variable strength. And so if they rupture or leak, whatever you want to call it, and they're contained, then you have a little bit of time. If If it's a free rupture, then they're done. They usually don't get to the hospital. They die at home or wherever they are.

So whenever you see this-- and the thing is, I always try to tell the OR staff, because we've become so casual in treating these with endovascular means. Everybody's stable until they're not stable. So it's one of those things like stop acting like you have all the time in the world. Let's pretend that he's actually dying, because he's about one bad second away from it.

And I'll get to that later on in my topic. The natural history of aneurysms is to expand and rupture. 50% of them die from other causes if they have an aneurysm, and 50% die from an aneurysm rupture.

So this was what I was referring to in terms of the role of gender in aortic aneurysms. The mean diameter preceding rupture in this patient [INAUDIBLE] cohort was 5 centimeters and comparable to 6 centimeter in men. So a smaller aneurysm in a woman is more worrisome than a medium-sized aneurysm in a man, for a lot of different reasons.

You have smoking on top of that, and that increases fourfold your relative risk of rupture. So here you see variables associated with aneurysm rupture over 1,000 patients. And if you look at the hazard ratios, the biggest hazard ratio is female sex, 4.5.

Age was not a factor. Size, 2.5. Current smoker, 2.11. Blood pressure was not a factor. So smoking and female sex, biggest predictor of rupture.

Some of you may be familiar with the Law of LaPlace, and Law of LaPlace basically refers to the tension, the pressure on the aortic wall in a linear model in a Newtonian fluid homogenous model where tension times radius equals pressure. So the higher the pressure, the bigger the radius, the higher the tension. So bigger the size, more the blood pressure, probably higher risk of rupture.

So this is the computer modeling I was talkinga about. This is finite element analysis, and what it does is it takes the aortic aneurysm and basically models flow through it based on certain assumptions that are made and looks at where the most stressors would be. And all of these color maps basically show you increased shear stress, decreased shear stress, and so on.

And then they correlate that with where aneurysms actually rupture. And it's usually the posterior lateral wall on the left side.

And based on that, they try to predict, independent of the size of the aneurysm, if you can model what the forces are on that particular patient's aneurysm wall to see when it reaches a certain point, is this more predictive of rupture, and should he be treated, or she be treated? And it has variable results, because this is all retrospective analysis. Nobody has prospectively said "aha," because you can't. You just can't get that kind of information. And it's interesting in terms of modeling and developing predictive factors, but it's never been validated in a prospective cohort of patients subjected to this analysis.

But it does show that if it's patients surviving, large diameter patients don't survive as much as small diameter patients. Those with higher shear stress-- we find there's more than 44 Newtons per square centimeters on a given aortic wall, then you're at higher risk of rupture.

And then if you have a small diameter and low stress, or a large diameter and low stress, the curves are the same. Retrospective analysis. And if you have a small diameter and high stress, and large diameter and high, stress are worse. So basically, it says, if you were to look at size, yeah, it probably matters, but what matters more is the forces on the aortic wall. And you have a high shear stress, then whether it's small or large, you're at a higher risk of rupture than a small or large diameter with low shear stress.

And these are the limitations of the biomechanical approach. You're not taking into account the wall, the thickness of the aortic aneurysm. You're not taking into account whether the aneurysm has thrombus in it or not, because most aneurysms have thrombus that have been laid down over the years, and that's probably predictive. If you see an aneurysm with no thrombus that's probably at higher risk for rupture. Just clinical experience tells them that.

And then there are differences in tensile wall properties. And there are a lot of assumptions in mathematical modeling that may not be valid to make assumptions of. And then this just refers to the biology. I won't go over the biology of aortic wall, but there is information in the aortic wall.

And there have been lots of studies that have shown that if you put patients on doxycycline, probably due to its anti-inflammatory properties, not its anti-bacterial properties, you can reduce the risk of aneurysm growth and rupture. Once again, it has never been validated as a strategy in and of itself, but it's been shown in animal models. And very few people have

extrapolated that to clinical modeling in terms of treating patients.

So information is important like it is in everything else. So if you want to put a schematic together, these are the factors that affect aneurysm growth and rupture. Genetics-- probably the biggest in terms of development of an aneurysm-- inflammation, smoking, aortic diameter, reactive species.

The inflammation leads to the aggravation of the elastin. So collagen gives the-- whether it's the aorta or any blood vessel the strength. Elastin is what allows it to expand and then recoil. When that elastin gets destroyed, the expansion continues to occur, but there's not that recoil, and so that wall become thinner and thinner.

And because the radius is increasing, going back to Laplace's Law, the tension on the aortic wall is increasing. So smoking causes this to be worse. If you don't smoke, and you have alpha-1 anitrypsin deficiency like you do in pulmonary disease, that causes that could be worse. Patients who have an aortic aneurysm have alpha-1 anitrypsin deficiency-- higher risk of rupture, like in smokers.

So what do we know? We know that aortic aneurysms are under-diagnosed and under-treated. The disease is much more common in men, but more dangerous in women-- a fourfold risk of rupture at a given diameter. The aortic diameter itself is an inadequate predictor, but that's the only real reliable metric we have for deciding when to intervene.

So natural history of the aneurysm, we know, is growth and rupture. But if one has an aneurysm, it's just a matter of when it will be fixed. So the conclusions from the small aneurysm trials are flawed, because it says smaller aneurysms, you can watch with surveillance. But most likely, what you're watching is them growing. So at some point, they're going to need to be repaired.

So this is the SAAAVE Act, which was signed into law by President Bush in 2006. And it's a one-time screening on Medicare entry for anybody over age 65, men who have smoked more than 100 cigarettes in their lifetime-- I don't know how they arrived at that 100 cigarettes-- and they're over age 65. You get a one-time ultrasound just to make sure you do or don't have an aneurysm.

Or women with a family history of aortic aneurysms. Anybody who has an aortic aneurysm-- there's a 15% incidence in first-degree relatives with an aneurysm, so you should counsel

them that they probably should be scanned at some point. First-degree relatives meaning brother, sister, daughter, son.

There are two way of repairing them-- open repair-- and I do mine retroperitineally instead of the midline. The midline approach is the standard approach. You go through the abdomen, you [AUDIO OUT] and blah, blah, blah.

I do it retroperitineally where I go through the flank, and their recovery is remarkably better. They're in the hospital usually for three to four days instead of five to seven days. I usually have them eating the very next day.

They don't have the illias. They don't get an NG2, et cetera. But it's a harder exposure if you're not used to it, so most people don't know or are not comfortable doing it. And there are no real anatomic constraints, as far as I'm concerned.

The other way is to do an endovascular stent-graft, which I'm sure all of you are familiar with, and that involves going through the femoral artery. And most of the time, we do this subcutaneously now. We don't even have to make small little incisions like we used to, unless there's something in particular about that patient's femoral, artery, disease or anatomy.

But the idea is it's a self-expanding graft with an impermeable fabric made of [INAUDIBLE]. And you deploy the main body, feed it below the renals, open this up, there's a contralateral gate. Come in through the other side, get into the gate, extend an additional limb, and then extend the limbs as needed. And that's sort of the general schematic of how one repairs an aortic aneurysm with an endovascular [INAUDIBLE].

But there are anatomic constraints that render the patients suitable or unsuitable. When we first started doing this, when I was a fellow in 1999 at UCLA, probably 40%, 50% of patients at best were candidates for this. And now, I would say probably 70% to 80% of patients are. And probably some people would push it even higher, but I think that's sort of almost a pseudo-religious approach, because everything can be done doesn't mean it should be done endovascularly.

To determine whether somebody is a candidate or not, in addition to the health features, the anatomic features of the aneurysm are very important. So you need a CT scan [INAUDIBLE]. So the things we look for is that the aortic diameter of the aneurysm has to be no more than maybe 30 centimeters, because our grafts only go up to 36 centimeters. So if the aorta above

the aneurysm at the level of 34 centimeters, then unless you do a fenestrated graft or something, which I won't get into here, they're probably not good candidates for a stent-graft.

You have to look at the distal aorta, make sure that there's enough room for the device to go up. You have to look at the length of the iliac arteries because you don't want to cover the internal iliac arteries, because you will get pelvic ischemia and colon scemia and all the rest. So there are a lot of anatomic features, so the CT scan is critical.

The other part of it is that the endovascular stent-graft reference is very cool, because you can do it, it takes an hour, or two hours. They go home the next morning, they don't have an incision, recovery is nothing. But you have to be committed to follow-up, because with an open repair, once you fix the aneurysm, you're fixed. You're done forever, you don't need surveillance, you don't need anything else ever.

With an endovascular stent-graft, you need continued surveillance basically in perpetuity. So for reasons that I'll get into in a second, if somebody's 50, 55, 60 years old and at good risk, I will tell them both options, but my recommendation is an open repair. Because you're looking at the next 30 years of some sort of imaging to keep an eye on the aneurysm, because people have been known-- there's a 1% risk of rupture in the literature, very reliable literature, 1% risk of aneurysm rupture after being treated by a stent-graft years down the line. That is the because of loss of follow-up in most cases.

What can happen? Well, you can develop what are called endoleaks. There are five different kids, but the first two are the most common.

Type 1 endoleak, where the stent-graft is attached here or here, if there is a leak around there, and that means the aneurysm sac is pressurized. So you never leave the operating room with a type 1 endoleak. You've got to fix that, because it means you really haven't treated the aneurysm.

Type 2 endoleaks are the most common. About 20% to 40% of patients will have type 2 endoleaks. And type 2 endoleaks refer to within the aneurysm wall, you have lumbar arteries, you have the inferior mesenteric artery. And when we do an open repair, we open the aneurysm, we close those. We suture them closed.

With this, we don't have the opportunity to do that, so those vessels can back-bleed into the aneurysm. So those are type 2 endoleaks. In the great majority of patients, they are benign.

As long as the aneurysm is not expanding, even if there's a type 2 endoleak, we just watch it. We just watch it with CT scans and/or ultrasounds. But if they are expanding, then you've got to do something about that, because that means that aneurysm is growing. And type 3 is a defect in the graft, either at the attachment site, or a tear in the graft. And type 4 is porosity, which you don't see any more.

So there have been three big trials looking at open repair versuss endovascular repair. This was the DREAM trial, which is the Dutch Randomized Endovascular Management trial. And it essentially shows two things, and the next two trials will show the things there.

Open repair, 4.6% mortality, endovascular repair, 1.2% mortality. Increased statistical significance, but there is a real difference. Operative [AUDIO OUT] complications-- 10%, including pulmonary, renal, all the rest. And 4.7% in endovascular repair.

So for the long-term survival, it's about the same. Endovascular-- this was the United Kingdom, Evar1 and Evar2 trial. Evar1 trial, in this particular slide, shows you that the survival of patients with aneurysms treated open or endovascularly-- the curves are exactly identical-- 93%, 93% endovascular repair survival from any cause-- 54%, 54%.

So this was followed out for eight years. So no difference is seen in total mortality or aneurysm-related mortality in the long-term. But in the short-term, in the 30-day, endovascular repair had a lower mortality.

And then this was the over trial that came out of the VA, which shows basically that aneurysm-related cause of death-- this is 30-day-- 2.3% in endovascular, 3.7% open repair. So American mortality statistics are much better than Europeans, and it's always been the case, and we don't know why. But there's a big difference.

But here's the thing. There's a 1.4% incidence of rupture in the endovascular treated patients long-term, whereas 0% in the open repair. So if they can't commit to follow-up, then endovascular repair has its limitations.

And then briefly, I'll just talk about ruptured aneurysms. Nowadays, we treat ruptured aneurysms with a stent-graft instead of taking them to the OR, unless they're in extremis, in which case you don't have time. If it's a free rupture, like I was referring to, you rarely have to have them get a CT. The hemodynamics are dire, and you just have to take them right away.

And if somebody shows up in the emergency room or in the hospital that has a ruptured aneurysm, their blood pressure needs to be kept low. You do not want to resuscitate them to 110, 120, 130, 140 millimeters to mark. We want them at 70 and 80, because the higher the blood pressure, the increased bleeding issues effect from the aneurysm rupture site.

So most patients, most centers, if you show up with a ruptured aneurysm, and you are quasi-stable, we will treat it with a stent-graft, assuming the CT shows that you can have a stent-graft. So a CT is critical. If you can't, then you do open repair.

So the question then-- and it's always a selection bias in case reports, because those who could had an endovascular approach. Those who couldn't went to the open. So the worst ones went to the operating room, and it's not surprising that we have worse outcomes than those who have time to get to the cath lab with an interventional suite and have the endovascular repair.

So this was the first trial-- this is called the IMPROVE trial-- looking at a randomization of patients with ruptured aneurysms to either the endovascular approach or the open repair. So there were 1,275 patients with admission diagnosis, 623 were randomized, 613 were eligible for repair. And here's the interesting part-- here's the endovascular strategy, meaning that they intended-- they intent to treat analysis-- they intended to treat these patients with a stent-graft. And some of them may have deteriorated on the table, may have been found not to be fit, and were converted to open repair.

So if you're looking just to treat analysis, there were 275 in this, 261 in this arm. 150 of these to the endovascular arm actually got the stent-graft, and 25% of them died. Endovascular approach converted to open-- 100% of them died, because something went bad. Those who were thought to be endovascular candidates, but were not and had open repair-- 38% died. And then those who didn't have any repair, 94% died.

And then the cumulative statistic-- 35% mortality in ruptured aneurysms in patients randomized to the stent-graft group. How many over to the open repair? 297 randomized.

And for some reason, they were given a stent-graft-- 22% died. The ones who had open repair, 37% died. No repair-- 100% died.

The operative mortality in the open repair [AUDIO OUT] 37%. So a properly done, randomized, appropriately adjudicated trial showed mortality 35%, 37%. Absolutely the same

whether you get a stent-graft repair or an open repair.

Now, there are other issues that may benefit endovascular repair in terms of ilias and abdominal compartment syndrome, and length of stay, and all of those things. But in terms of pure mortality, there was no difference. There was no difference in 30-day mortality.

Also, length of stay varied. And endovascular repair is more expensive than open repair. I published a paper when I was a fellow at UCLA looking at this even in 1999, and the concept was, well, hell, you're doing a stent-graft.

They're out of the hospital in one day. It's got to be cheaper than a seven-day hospital stay. It was prohibitively more expensive to do a stent-graft repair because of the cost of the device. Accounting for a seven-day hospital stay in the open repair, pharmacy, medications, all the rest.

And then I remember the concluding statement we wrote that hopefully with more products coming in, there will be more drop in-- uh-uh. The expense of the stent-graft has continued to rise, and rise, and rise. And to this day, from the hospital perspective and from the insurance perspective, an endovascular repair is exquisitely more expensive than an open repair. Even accounting for a seven-day hospital stay, when most of us who do it retroperitineally, they're home in three to four days.

Selection bias is always present when studies are not randomized. That's why the improved trial and all the others are so useful, because it takes most of your assumptions. And as Aldous Huxley, said, "The great tragedy of science is a luminous theory slandered by ugly facts." And this is an example of that.

So the approach now that I take and that I'm trying to institute here at John Mirror is if you have back pain, hypertension, come in, and you thought you had an aneurysm, you get CT confirmation of an aneurysm rupture. If they're stable for endovascular stent-graft, you go to the cath lab. If you're not, you go to the OR, and here's all the logistics about-- you guys all need to know this about who to call and how to notify.

This is the ideal situation, a hybrid operating room where you can convert from one to the other seamlessly. We don't have such a thing. I need to confer. We have a-- room 5 is called the special. It's not truly a hybrid OR, but we can use it as an OR for limited purposes.

But this is ideal for these kind of cases. There's just a final picture of a ruptured aneurysm that

I did in-- this was before. Thank you.