When to Consider Procedural Closure of the Patent Ductus Arteriosus in Premature Infants - Pediatric Grand Rounds Meeting-5-23-25

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58m 22s

Kamat, Deepak M started transcription

Ted Cieslak 0:07
Much.

Kamat, Deepak M 0:36
Good morning.
It's 730 in San Antonio and it's time to start our pediatric grand rounds.
The CME code is in the chat box, and as always, we'll repeat it every 10 to 15 minutes.
But Antonio Hernandez will be introducing this morning's grand rounds speaker.
But Hernandez, go ahead please.

Antonio Hernandez 0:57
Good morning, everyone.
I'd like to welcome Doctor Phillip Levy.
Doctor Levy is a neonatologist at Boston Children's Hospital and associate professor of Pediatrics at Harvard Medical School.
He did his pediatric training at New York Medical College in Westchester and then completed his neonatal Perinatal fellowship at Wash U in Saint Louis.
He is currently the Co director of the PDA Preterm PDA closure program.
And is the clinical liaison between the division of newborn medicine and the heart Center at Boston Children's.
His academic focus is neonatal hemodynamics, PDA management, bpd bronch pulmonary dysplasia, and occasionally on the side, he said.
He does a little hyperbilirum anemia.
He has built a pretty robust PDA closure program, coordinating PDA management with 16 different medical centers across New England. He set in on over 100 Cath Lab PDA device closures and today he's going to share his insights and work on current

evidence on PDA device closure, so.
Please welcome Doctor Levy.
Thank you.

Philip Levy 1:56
Thank you, Antonio, for for that wonderful introduction. And really this has just been a wonderful trip. I'm sitting in in my hotel room in San Antonio, but I've had the pleasure of spending the last several days here with the Group of neonatologists at your hospital and just kind.
Of blown away by the the sheer size of the hospital and also kind of the growth and all of the different rooms that you have there.
Really to care.
For the sickest babies, not only in your hospital, but also all of the care that Antonio and his team provides with with transportation.
So I know there's a potpourri of of of clinicians and physicians on this call today.
I really wanted to highlight really a a novel.
Non invasive approach to mitigating the negative effects of the inductus arteriosis and premature infants. And if you are a general pediatrician out in the community.
You may say, why would this impact my practice?
But you're gonna see more of these children who have these devices, and it's important to understand where they came from.
So just some disclosures and disclaimers I am involved in some different grant opportunities and I am fortunate to to work with Abbott and then my disclaimer as I pointed out over the last couple days is I have three boys.
A 14 year old.
A 12 year old and an 8 year old.
And they were 5-6 years younger during COVID.
And I had tasked them with making bitmojis of me.
So hopefully if you're driving, if you're at home wherever you are, you'll at least pop up when I put some pictures on the screen and my middle son made this picture of me 'cause, he knew I was going to Texas with my, with my cowboy hat on, so.
This is a call I got from a local pediatrician about 3 weeks ago.
It was a four year old former 25 weaker.
And she asked me what is?
What is this in the chat?

And just to highlighted here, basically she had noticed that there was something in and around the PDA and I said, oh, that's that's a that's a a device that's a piccolo device that that we put in that baby, you know, four years ago.
So I figured it it was only that I got the call and then I was going to be able to give this kind of this talk.
So this is is what the device looks like and I'll have several pictures throughout the talk to talk about.
The impact of the device.
Outcomes related to the device when we consider placing the device, but it's a device that's placed.
Via kind of trans catheter approach and I'll show a picture in a few minutes of of Doctor Heibel and the work that she's doing down with your center. So rewinding, you know, four years prior, the calls that we get at Boston Children's and we're a freestanding child.
'S hospital.
We have a 30 bed niku.
We have all referrals in is we get a call about a.
Former 25 weaker, whose 12 days of age, who still is intubated and has respiratory distress syndrome and seems to have.
Apda that is large and in charge as I like to say and causing some hemodynamic insignificant significance. And the team has kind of tried some Tylenol, which I'll speak about in a few minutes to augment closure and the questions that we get with our consultation team is should.
We try another course of pharmacotherapy.
When should we think about referring to your program for definitive closure?
Which could either be a surgical ligation or device closure and is the baby even eligible for device closure?
So I'm going to kind of walk you through some of that, but I'm a big history guy and I I love the history of PDA closures and it to me, it's really fascinating.
So basically the idea of closing the PDA started in about 1888 with John Monroe, who was a cardiologist.
He disse.
Out the PDA in an infant cadaver.
And then he failed at trying to convince the pediatricians of its importance.
And you can see here Fast forward 100 plus years. We're we're still kind of in that

tussle between understanding its impact with cardiology and neonatology.
He published a landmark paper in 1907 at the Children's Hospital of Philadelphia Conference, really highlighting.
The role that litigation could play of the PDA.
Now it was really.
To prevent endocarditis in children at that point and for 31 years, multiple individuals try to close the PDA.
But they all failed.
And it was until 1938 when Robert Gross, who was a resident at Boston Children's.
And this is really the start of congenital heart surgery and and surgery throughout the world.
He suture closed APDA and a 7 year old, and it was fascinating because he put two individuals on.
The Ork schedule.
For that day, the thought process was that if the first individual passed away or died on the table, he would have a backup option and even more concerning was that he did this while his mentor, William Ladd, was away on holiday in Europe.
Because William Ladd was vietnames opposed to it.
So for all the trainees who are on the call and all those people out there, I don't suggest trying to perform procedures when your senior mentors are out of town.
But it wasn't until Werner Portsman in 1966 when he.
Was doing an intervention.
He basically put a catheter through the PDA with kind of a device and it basically noticed that the heart sounds got muffled and they kind of went away when he had that catheter through that PDA.
And he thought, MMM.
Maybe there's a way that we can close the PDA permanently without doing the surgical ligation?
So he actually used an 18 French sheath which is about the size of of your thumb, and you can imagine.
Putting that.
At 18 French sheath in in a very premature baby in a vein. This was done in an artery.

TC **Ted Cieslak** 8:00
Derek Drake.

Philip Levy 8:02

That's really just not possible.
So over kind of the next 50 years or so, people like William Raskin really revolutionized the field, getting the right catheters down to much smaller size, where today we're actually using a four fret sheath. So 1/4 of the original size and we're doing it in veins rather.
Than arteries.
In the 70s into the 80s and 90s and the early 2000s, we introduced indomethacin. Ibuprofen and Tylenol, which are medications to augment closure and then in 2019 the FDA approved the first device to put inside a premature baby down to 700 grams. That would allow us to safely close a PDA with a device in the kids that warranted it.
So what I want to answer today is should how do we define the PDA that's causing issues?
What are our screening practices?
What are the initial approaches?
Because it's really important just to understand.
Where we all start and where we all go. Every baby is different, but the starting point could be the same.
What are the trends for device closure?
Are we doing more device closures or more surgical ligations?
And finally when when.
As a neonatologist or somebody out in the community caring for these babies, when would you consider referral for device closure?
So take a step back.
There's an evolving field.
In neonatology called neonatal hemodynamics, it's really a way.
For neonatologists and pediatricians to provide comprehensive physiological based approach for looking at babies who are at risk for cardio pulmonary disorders, it's a combination of using echocardiography therapeutic agents and understand the Physiology. And when I started trading back in 2004, 2003 when I thought.
Hemodynamics I thought of the PDA and pulmonary hypertension and blood pressure support.
But what I've noticed over the last 20 plus years or so is that it's much, much more

than that. It's simulation.
It's AI.
It's transport, its delivery room management, its congenital diaphragmatic hernia.
Now, as a general pediatrician, all of these babies will have the diseases early on, but they'll be tracked into young childhood and early adulthood.
And there's multiple kind of overlapping areas with point of care, ultrasound and transport.
I mentioned that.
And then there are multiple programs.

Antonio Hernandez 10:26
OK.

Philip Levy 10:27
That are starting up that allow neonatologists to become extra specialized in this hemodynamic care.
And there's even basic science translational efforts, genetic efforts, ohmic efforts, all the work that you do down here with your baboon and your labs.
So I just think there's a growing role of hemodynamics in the field of Pediatrics.
So for me, just taking a step backwards for a second.
A PDA, a physiological PDA patent ductus arteriosis.
We know that in a term baby, it closes within about 12 to 24 hours physiologically in an anatomically closes within two to three weeks. But in the younger, smaller babies it can stay open. But APDA is just a ductus that remains open beyond its developmental role it.
Not necessarily causing problems that needs to be addressed.
It's the pathological PDA.
So the Pda's that are significant are not just PDAs that stay open.
But refers to what?
The volume of the shunt is so large that there is so much blood going from that kind of out to left ventricle, shunting through the PDA into the pulmonary circulation, filling the balloon aka the lungs with water. And it's going to cause cardiovascular compromise.
The challenge is that the timing of the intervention, when we need to either give pharmacotherapy or definitive closure with ligation or device is based on what I call

the total.
Assessment of both how the baby looks and is doing based on the neonatologist interpretation and how the Echocardiographic findings based on the cardiologist interpretation and then the expected course.
So very briefly, for those who like echocardiography, what we do is we look at the ductus arteriosis.
We can look at the flow patterns. We can see if it's restrictive.
So that means there's not a lot of blood flow going necessarily into the lungs or non restrictive. We could look at.
The degree of the flooding of the lungs pulmonary over circulation.
We could look at how much blood is being stolen from the systemic circulation.
So we call it hyperfusion or the descending aorta.
We can look at the health of the heart and then we match it up with the clinical features. Is the baby intubated?
Is the baby on high support?
Does the baby have kidney injury?
Is there interventricular hemorrhage, necrotizing enterocolitis?
How is the stealing of blood from the systemic circulation impacting the overall health?
Of the babies. Here's here's a little caveat.
Not all PDAs do this.
They don't all look like a damn that's about to burst or bursting. We know that babies who are greater than 28 weeks gestation.
The chances of them having a hemodynamically significant PDA are very rare.
This is really a disease of the extreme premature infants. We know that the natural course of most of the Pda's, 20 to 30%, close by two to three weeks.
4050% remain open, but actually.
Don't cause any clinical problems, even though they may look like this picture on the left or right of your screens.
But it's the five to 10% that are causing the issues and that's where we're spending most of our time trying to understand who should we be treating either pharmacologically or with definitive closure. And as I mentioned, there's increased risk of morbidity and mortality only in the Bab.
Less than 26 to 28 weeks and only in the.
Moderate to large high volume shunt so looking like this dam with that's breaking

through.
So just as a quick review, most of us learned this back, you know, in medical school and then it's refined when we do our pediatric rotations through the NICU. But there are several options to attenuate a PDA that may be causing issues. You could medically manage this with.
Nutrition, which is above all the things I've done in my career, that's probably the number one thing that has advanced the field of neonatology, fluids, diuretics.
Optimizing the respiratory system.
There's pharmacotherapy, which in 1976 indomethacin.
And then 95 ibuprofen, which acts on the Cox two inhibitors, which helps promote ductal closure.
There is Tylenol which acts on the pox side of that pathway. Up until 2019, the only choice really for babies.
Less than two kilos were surgical ligation.
The choice for babies over 5 kilos had always been transcatheter closure, but with the FDA approval of a device down to 700 grams, we now have this option to close the PDA.
With a trans catheter device.
So here's just a picture.
From from from the Abbott company, and basically I'll walk you through for those who have not actually seen the procedure, it's, you know, here's a picture of the heart.
Here's the PDA going from the pulmonary artery to the aorta and basically using a minimally invasive. This is what the the the device looks like. One of the devices, usually a minimally invasive approach going through the the vein.
We're able to go up through the IBC to the right atrium, to the right ventricle. We place a catheter through the PDA and using both echocardiography and using angiography. And I encourage all of you to reach out to doctor Heibel as she builds the program here we're able.
To then place a device intralumerally within the PDA. This device specifically has kind of three rings. You can see there.
And using echocardiogram and angiography, we're able to look at the placement of. Of the device we want to make sure it's not sitting too far to the aortic site, causing a quartation like or the pulmonary side causing kind of stenosis or compression. And basically they were able to see that no longer is the blood flow going through the

PDA and.
Everything looks kosher for lack of a better word here I just put this up.
Here is doctor Haibel.
I don't know if she's on the call, but I had the opportunity to spend the last couple days with her and the team and doctor Hernandez and really there is.
Such opportunity.
To provide really the highest level of care and what I what I tell people is this is just another tool in your tool bag and as clinicians and pediatricians, there's going to be stuff in this talk that resonates.
There's going to be stuff in this talk that you don't agree with, but overall, when we counsel our families and these sickest babies, we need to make sure that we're providing them with all of the information, regardless of our personal opinions regarding the PDA, which still 3040.
Years later, remains one of the most controversial.
Topics in all of Pediatrics.
So again, I highlight the work that is ongoing in your center and the work that doctor Haibel is bringing to you guys.
So. So these are just kind of some pictures of of what? What Doctor Haivell will be doing over time is, you know, here's a catheter that's going through the tricuspid valve, the right atrium. Right ventricle.
And here's a wire that's able to then go through the pulmonary artery, through the PDA and into the aorta.
And then what?
Is what we're able to do again, there's many different variations.
Of this, but this is a delivery system where we're going again up, right?
Atrium. Right ventricle, through the pulmonary artery, through the PDA and then through the aorta in order to get all of the different landmarks that are then needed to identify the right location for the placement of the device.
Then they're able to use kind of contrast here in order to get a really good understanding of what are the landmarks.
Of the PDA.
And again, this is a little bit beyond what I do on a day-to-day basis.
I am a neonatologist and I am always amazed at how doctor Heibel and her team is able to take a kind of a 2D image and make it a 3D structure.
But they're able to do this successfully.

They know what the landmarks are, and then it's really just totally remarkable what they're trying to do is they're trying to place a device perfectly inside that PDA where it's not sticking out.
Towards the pulmonary side or it's not sticking out to the aortic side?
And then using angiography and echocardiography simultaneously, they're able to then kind of place this device. And and here's just an example of how technically doctor Heibel and her team would slowly get the catheters in the right position.
And it's a very technical skill. We're slowly pulling back the catheter and really trying to get that device and and and let the device come out of the catheter first.
There's a first disc that's coming out you can see.
Here and then there's a second disk that's gonna come out this middle disk, and then finally what you'll see is the whole disk.
The third disk comes out really and then and then what you're left with over here is really attached to the catheter.
It's kind of shapeding back and forth.
Here is the device intraluminally inside that PDA using echocardiography and using angiography able to really assess is it in the right location.
And and basically, here's just a picture of the device.
Perfectly inside the PDA.
We don't want it to be LPA obstruction or even aortic obstruction.
And what's novel about this procedure for those who have not seen it? We don't need arterial catheters.
There's no retrograde aortogram that we need to do so.
There's no.
Insult to the to the any of the arteries which is really novel 'cause these doing this in a 700 gram is challenging.
It's fluoroscopy guidance and it's echo guidance and its reliance and even some centers do it in the Cath lab. Some centers do it at the bedside and some centers even go out to the communities and do it, which is a whole nother discussion and processes, but just knowing.
That what I want to kind of do is focus the rest of the talk.
Not on the decision.
Close the PDA how you got there.
But somebody has made a decision that the PDA is a problem causing lung issues, body issues and it needs to be closed.

So you are beyond that fork in the road.
So So what does the data say? So in 2019, with the FDA approval of a device down to 700 grams in premature babies.
You can clearly see from our own Boston Children's data.
And our own.
And and then the national data that there was a rapid rise in device closures highlighted in blue circles and a rapid decline in surgical ligations where some centers don't even offer a surgical ligation anymore. For those babies who need definitive closure.
Ed Rewindy our case the the question becomes for us is you caring for that 18 hour old 800 grand baby?
The baby's intubated.
The baby has respiratory distress, has all the comorbidity risk factors you read about in neonatology. And the question for us becomes when would you start looking for that PDA?
What we know in general is that APDA that remains open with a left to right flow shunt and floods those lungs has been associated with worse morbidities.
Bronchopulmon dysplasia, intra ventricular hemorrhage, necrotizing enterocolitis.
Long term now, yes, the data is not yet fully there to say closing the PDA and all of these babies decreases these morbidities. But in some babies those two to five babies out of 100 that I mentioned, we need to figure out how do we screen for.
Them and how do we follow them?
So there are two different approaches in the field of neonatology.
You can use what I call a risk based assessment or you could do it based on symptoms.
So there are novel programs around the country where neonatologists.
Are doing their own bedside echocardiography and they have the capability of doing echos on the smallest babies and they decide to do the echos based on the risk and the risk often is is the baby mechanically ventilated.
And they're gestational age thinking that babies less than 26 weeks or higher risk compared to 27 to 29 weeks.
So they'll do screening.
As early as one to two days of age and the higher risk and then?
Three to five days in the lower risk, the majority of centers around the country don't have that option to do this.

So they screen based on the symptoms.
So do you have increased respiratory support?
Do you have the classic widen pulse pressures because the blood is being stolen from the body and going into the lungs so the body lowers its defenses?
Do you have metabolic acidosis?
A hyper dynamic pricing, do you have a murmur?
Things like that.
And then there are some babies.
Who don't have any clinical signs throughout their NICU stay, but the echo persistently shows a PDA that's large.
And those babies may come back at six to nine months of age, or even older into Doctor Heibel's lab, and she will close these babies PD as when they're in infancy or young childhood.
So basically what the kind of consensus statement says from the Canadian Pediatric Society is that if you have the capability of doing routine.
An echo in the 1st 72 hours for those babies that are higher risk less than 26 weeks, you could consider doing some earlier screening.
We looked at our own data at Boston Children's.
And we looked at the chnc, the Children's Hospital Neonatal consortium.
Most people are very familiar with the Von Network.
So basically, the majority of center screen late in the first week at about 57%.
Our own data from Boston Children's.
And we have two really high level delivery hospitals that we work closely with and this was done by a fellow now faculty member at Emory. Our median time to check the PDA is about four to five days of age and our overall success rate is about 60%.
Using pharmacotherapy and I'll talk more about this in a few moments.
So now you Fast forward a little bit. You got that twelve day old baby.
And the question is, what would you do? You failed. Pharmacotherapy.
The creatinine is 1.2 and it's rising.
Would you do a conservative approach?
Would you do a trial of another course of pharmacotherapy or would you do definitive closure of the PDA so these are the questions that that need to really be thought about.
So pharmacotherapy versus conservative therapy, if you know the PDA is going to close on its own, some people will say I don't want to even try and treat with

pharmacy.
Or definitive closure.
So what the data says out there is that if you have a preterm baby and you have a PDA, that's an issue.
And clinically, the baby's OK. You could actually consider to just watch the baby for the first two weeks of age. However, if you're less than 26 weeks and you are on respiratory support out of proportion and you have end organ dysfunction, so you're stealing blood away.
From the lungs.
From the body.
Excuse me? Those are the babies that you shouldn't necessarily wait on that PDA 'cause it may actually cause some short term morbidity.
So those are the babies that we suggest considering pharmacotherapy to augment closure of those babies, Pda's.
So then the question is how many courses would you try and do? So the general teaching.
Is this there?
Are Cox two so indomethacin and ibuprofen and acetaminophen, which acts on the pox inhibitors?
That are shown to be effective about 60 to 70% of the time, but this rate declines with each course.
Now there are some data out there that usually more than two courses of these medications are not really advised.
Tylenol. You might be able to consider more than a second course, but there is some data trying to potentially connect Tylenol with some adverse effects, not only on glucose on long term morbidity.
So. So the jury is really still out there.
I tell my colleagues.
Is that you probably should think about one to two courses of pharmacotherapy before definitive closure.
And if you're waiting and there's insurance issues, a third course of Tylenol right now is likely not harmful.
But we need more data out there to understand the trajectory.
Here's just a recent study which highlights this really great point, the majority.
Of babies, 62% will get their PDA closed on the 1st course, but.

That clearly drops to 25% and then down to 8% on subsequent courses.
So if you truly have APDA, that's an issue.
You have to think long and hard on the amount of courses of pharmacotherapy you're going to give to this because they're not all benign. And if the PDA is really an issue and you failed that first course, you may be pushed to just go for definitive closure.
In our own data set and the national registries we use about two courses.
Of pharmacotherapy. Before we go on to definitive closure, really highlighting the recommendations that were made and now we have the evidence to match those recommendations. So that brings me to the next question.
So is device closure even feasible and safe? This data came from the FDA.
This is the data they used to really provide FDA approval.
They had 200 infants.
Less than kind of two years of age.
Less than a year of age.
Excuse me.
And a hundred of them were less than two kilograms.
You can see the median gestational age was about 25 weeks and the time to implant was right over a month.
And they looked at all of these adverse events, you know, were these babies able to get a device?
Did they have any major complications?
Was there any Caucasian?
Was there any LPA stenosis? And the answer was for the most part, these babies did extremely well.
The device or the Piccolo offered clinicians a minimally invasive option.
For closing a PDA that's causing a problem, but initially its effectiveness in improving the outcomes was unknown. So of course you needed follow up studies which again these investigators did very nicely. The three-year follow up studies looked at these babies.
They had no kind of residual shunt.
You can see red is bad and green is good and the overall mortality not related to the placement of the device was extremely low. So really there's low.
These complications, the survival rate at three years of age, was greater than 95%, which is probably standard of care for most babies less than 28 weeks. And the

conclusion was that device closure is still effective in safe therapy in preterm infants.
So a really nice paper had come out using cardiac catheter based data from the Impact registry. They looked at 1500 babies who underwent device closure over a long period of time.
The feasibility was 95% and the major complications was down to 3%, such to the point that over time individuals like Doctor Haibo's able to do device closure in the smaller and younger babies and it's the high volume centers that have kind of the best.
Outcomes the outcomes were not related to gestational age or weight, but more to the centers that do the high high volume. And just like what you're doing here. We did this in Boston the first several cases were babies greater than two kilos.
Then we move down to babies less than, greater than 1K, and then after we had about 20 or 30 under our belt, we started to move below the 1K mark and I'll show some data. The youngest we've done is 10 days of age and the the.
Smallest we've done is is about 560 grams.
So the conclusion here is if you have institutional experience like you have and patient characteristics are suitable, these are the babies where device closure may be considered as an alternative to surgical.
So in 2019, based on all the data that was available, we were tasked with building APDA closure program and the goal was to kind of close the PDA and we had to overcome some obstacles. There are some people that I, I don't mean to label them. But they're kind of wicked witches and thankfully, people like Doctor Heibel and others have come along, and I think there's a new wizard in town. What I like to call the interventional cardiologist where we have this new tool in our tool bag.
And this was made by my 14 year old and.
My 12 year old said I could do better dad and said it's not the wicked witch blowing away in the wind. It's the house that's falling on the wicked witch. Either way that you slice it or dice it, I think we have a new tool in our tool.
Bag that really needs to be investigated and what we did at Boston Children's and this has been done in multiple places. We built APDA closure team where our goal is to really close the PDA in the least morbid way possible.
This doesn't mean a device or a ligation, or even pharmacotherapy.
We act as a consultation service and I'll show some data in a few minutes.
We're 30% of our babies who get referred actually do not need any type of intervention in the PD as close on our own.

It's multidisciplinary, involving cardiology, neonatology, respiratory therapy, anesthesia.
We have a whole research arm, which I'll speak about at the end.
We refer from 16 centres around the New England region and we are constantly maintaining these relationships.
With educational webinars we do a lot of research and Qi initiatives.
Together we built a really nice team where the initial assessments are made jointly between the outside hospitals, neonatology and cardiology team. They make the referral to us our cardiologist.
So doctor Heibel would be the example in in this case and a neonatologist, let's say Doctor Hernandez would then Co look at the baby both clinically and echocardiographically.
If the baby's not eligible for device closure.
That we have act surgeon on hand, who's able to help us. And if the baby is eligible for device closure, we bring the babies in, we assess them.
We have a full gamut of anesthesia, respiratory therapy and nursing that helps us understand how to manage these babies safely from the Cath lab back to our NICU.
And then we have a post resuscitation kind of management plan where we try and mitigate the short term and long.
Term impact and the goal is to get these babies back to their referring.
Institutions or back to their baseline within two days post the procedure.
Other centers have followed suit.
This is from Atlanta and I'm happy to share all of this data after the talk, but basically they instituted a program where they have checklists. Now that you have epic, you can devise checklists within epic and basically, since they institute the program, they've seen a rapid rise in.
Their amount of PD as that they're able to close 'cause they have an infrastructure with a dedicated nurse.
Practitioner and research assistant who's able to do all the coordinating from insurance to follow up these patients long term and we're able to work with societies to develop guidelines based on all of our work where we're looking at patient selection, which is really based on the clinical and.
Echocardiographic features the joint assessment with cardiology and neonatology, and then our transfer processes, clear communication and all the transport considerations.

That doctor Hernandez and his team would be handling now. These babies aren't the classic sick babies. I've learned from him that are coming.
You know emergently these babies, you have time. They're planned.
The transport is smoother, so here's our data. You know, since 2019 we've had 265 referrals, as I mentioned, 30% don't actually ever come to us, which is kind of reassuring that we're able to kind of have people work with us and.
Do early referrals.
Of the 191 that went.
For definitive closure, we've done 157 calf procedures. We've had 11 babies who have deceased, none related to the closure itself.
We had one baby die within kind of the first week after closure. That baby had sepsis and all the other babies died much later due to other comorbidities related to newborn medicine and neonatology.
So for us, the feasibility is close to 97%.
We've done 152 out of the 157 were able.
Able to leave the Cath lab with a device.
One baby actually had no PDA when we went into the Cath lab.
So now we get echocardiograms on the mornings before we do the device closure.
A couple of the Pda's were just too large, and we tried to put a device, but we couldn't do it.
So the babies needed surgical ligation.
One baby had a pre operative complication, so now we actually intubate all the babies with our cardiac anesthesia colleagues up in the NICU.
Here's our experience and feasibility.
So our median time to close is about a month of age. Our weights about 1.5 between 1.2 and little larger, the youngest we've done is 10 days and the smallest we've done is 560 grams.
It's also extremely important that we report our complications, which are very much in line with what is reported in the literature. We have had babies.
Whose the disk has gone on the aortic side. We've had babies with the disk has gone on the.
Pulmonary artery side.
We've had some kind of thrombos one may be needed.
We had one baby who needed the device to be removed at nine months of age, 'cause it had moved on to that aortic side. And basically I feel it's really important to

report the adverse events. I will say that the adverse events on a whole are much less. Than the adverse events that get reported with surgical ligation. And while I would have loved to do a head to head.
Randomized controlled trial of Lipatient versus device closure.
The ship has sailed because most people, actually majority of senders, no longer even perform surgical ligations anymore. Can we do this down to 700 grams?
The answer is yes.
There are some caveats I think. Overall, if you go below 700 grams, which I think your center will get there for sure, it's really about.
Doing it in a situation where you have a high volume of center.
It's not related to the age or the weight. It's related to the technical skill set of the person putting it in in the high volume.
So the majority of adverse events and bad outcomes that are reported in the literature are related to the low volume centers.
So there are technical success around the country with babies who've had APDA device closure in under 700 grams.
So the question that people ask me really is, would you do surgical ligation?
Or catheter intervention.
As your primary choice, if you're going for a definitive closure, and as I mentioned, most centers don't even do surgical ligation. But from retrospective datasets, there was a nice meta analysis that came out that basically concluded that device closure compared to ligation leads to less mortality less post.
Closure syndrome, which I'll speak about in a few moments.
It protects against some of the morbidities of neonatology like Periventricular leukomalatia.
Or retinopathy of prematurity. There doesn't seem to be a major difference with some of the other ones like bronchopulmonary dysplasia or chronic lung diseases.
But the babies do wean to excavate quicker.
And the cost may be the same, but the overall ICU length of stay seems to be less.
And we did a study several years ago looking at cost analysis and propensity scoring and that also bore out as well.
So Full disclosure, some babies still need a ligation.
I I don't understand how some centers don't still have this in their tool bag, but for us it's really the baby who has an active necrotizing enterocolitis where there could be a surgical perforation of the bowel and it's due to the steel effect from that PDA

where you.
Have evidence of lactic acidosis.
And organ dysfunction with acute kidney injuries.
Those are really the kids that I still would not wait to do a device closure because you're not going to put a device in a baby who has an active infection or active concerns.
The other two in our kind of cohort that we noticed post 2019, so unfavorable morphology and active infection with time, the infection will get better and we've waited two weeks allow the infection to simmer down and we do device closure now and then the unfavored Mor.
As you become more proficient.
Our interventional cardiologists are just so much more adept at handling this unfavorable morphology.
And we're usually willing to try device closure even if the PDA doesn't look like it may be amenable on ecka.
And we've been pretty successful at this approach.
So the question that I always get is what's the optimal time to do the closure?
So if you have APDA that you know that needs to go away, and that's that's a challenge cause which of those are the PD as that's a whole nother talk. But basically there are three studies out there that have really honed in on this four to six week.
Period or less than 34 weeks post menstrual age.
So the first study came out of Memphis and what they basically showed is if you have APDA that needs to be closed and you close it under four weeks of age, that's Group 1 here.
Those babies extubate quicker.
And their overall respiratory symptoms seem to improve quicker than if you had it closed at one to two months of age or you had it closed beyond two weeks of age.
So this was a nice starting off point.
I think we as neonatologists don't fully appreciate what the catheter interventionists need to go through. While it's easy to say, just wait, wait, wait.
The most challenging babies to put APDA device is actually the babies. Between about 1.52 kilos all the way up to 4-5 kilos.
Because the PDA in a premature baby is long and skinny.
Kind of here this fetotype.
Over time, they become more like type B or even type D or type C.

So basically it narrows down and it can become a little bit harder at different time points. So basically.
The INTERVENTIONALISTS wanted to look at the data.
Who are the kids that have better outcomes based on their morphology?
So a group from Atlanta actually looked at this question.
Exactly what they found is the babies who have the type F so those fetal type ones that that we find the majority of premature babies, their PD as were closed at about 5 weeks of age, less than 34 weeks. So about 31 weeks Postmenal age their.
Time in the Cath lab was less and their overall adverse events where the device moved or there was embolization was also less so.
They basically concluded that the ideal time point.
From a morphological standpoint, to close APDA that is an issue is really less than 34 weeks. I say less than 31 weeks and less than about four to six weeks of age, which really goes along with the other data in Memphis and what our own group.
Did was we looked at our own data and we basically did some what we call targeted emulation trials, which is using some novel statistical approaches and AI.
And we basically said from the time that you get referred.
To the time you get your PDA closed and babies.
Who that time period is less than four days of age.
Their cumulative incidence of extubation was actually higher.
So the babies who get referred to us and have the PTA close relatively soon after they're able to extubateway quicker. The babies who get a device are able to extubateway quicker. And to me, what we've also learned in a subset of babies who come to us less than.
2-3 weeks of age.
And get a device closure.
In less than 4-5 days of age, those overall outcomes seem to be more improved than if you wait and sit on these PDAs.
So what we tell people is not necessarily when to close the PDA or what drugs to use.
What we try and tell people is if you have APDA that's causing you an issue, early referral and timely closure is ideal. This procedure is another tool in your tool bag.
We a neonatology are very adamant that my way is.
Best way?
But what we need to start thinking about is what's best for the baby and what's best for the baby is really providing all the tools in the tool bag to the family. You can

decide to watch the PDA.
You can do pharmacotherapy.
You cannot do definitive closure, but at least you've presented all the options in a fair and honest way, and that's one of the take home messages of this talk.
So the last kind of couple minutes before I answer questions, I'm just gonna walk you through how I think about considering, you know, PDA closure.
So as I mentioned, there's several different ways to screen.
So if you're in a program that can do hemodynamic screening in the higher risk kids, you may get an echocardiogram in the first couple days of age.
You may see that the PDA is an issue.
The baby may be intubated, and then you may start some pharmacotherapy.
Tylenol, which is a seven day course. You check the pdaa.
Few more times over the course of that first week, let's say the PDA is still causing an issue.
Then you start another course of Pharmac.
Therapy that the teaching is if if the first course doesn't really budget the PDA, don't use that same first course again.
Switch pharmacotherapy courses.
And that would mean the earliest I would consider doing device closure is around 10 days of age in this kind of paradigm.
Let's look at another paradigm.
You have a lower risk, baby, so you get an echo a little bit later in the first week of age.
So you have clinical symptoms. You know you're intubated.
You may get a few.
Echoes. Start some Tylenol.
So in this situation, the earliest I would actually consider device closure if the PDA is an issue is again around 10 days of age.
Some people may do another course of pharmacotherapy.
That's at your discretion.
Now you have this data that's actually come out.
It's really fascinating in centers that have these types of programs. What they found is that when they do the hemodynamic screening in the smaller, younger babies, they found that they're giving more pharmacother.
Therapy, but they have less babies going for device closure or definitive closure in

babies. A little bit older they found by screening earlier, they give less pharmacotherapy 69 to 85% and they do less definitive closures.
And this study is not novel because these babies also had less ivh less neck and less death.
So there is something to be said about having.
Screening programs in the highest risk babies, but I will argue that the majority of centers.
Like my center and your center, we scream based on symptoms.
So a baby's intubated.
They have a murmur.
We get an echo, then we start some Tylenol and we do some more echoes.
So the earliest I would consider doing device closure here is about 10 days of age.
You can see that 10 day Mark is really highlighting here.
There are some centers out there that refuse to check the PDA in the first week of age because the overwhelming majority of Pda's will then close.
Or not 'cause an issue?
So in this paradigm, what they do is they'll only check for the PDA if there are risk symptoms like respiratory distress or still mechanically ventilated, and if they get an echo, the earliest that they would consider device closure again. Is that really 10 day mark. So really we.
Highlight the 10 day mark. So for me, you know the the 10 day Mark is really that's the real kind of crux of the issue.
So who would I close the PDA in?
Those are babies less than 28 weeks.
When would I do it?
You know greater than 10 days of age.
Still mechanically ventilated, I would try up to three courses.
Really one to two courses of Pharmacare therapy and in a center like yours and mine, I would do device overlaysion when institutional experience is present.
Now, one of the major complications is this thing called post ligation syndrome.
So basically, if you follow me for a minute.
When you have APDA that's open, all the blood leaves the left ventricle, goes through the PDA and floods the lungs.
So basically have less blood going out to the body and more blood coming into that left atrium.

So the left atrium gets big and dilated. If you do definitive closure with a clip or a device no longer is the blood going into the lungs, so no longer is it coming back to the left atrium.
So that's a decrease in preload.
All the blood is now going to go out to the body.
And when it goes out to the body, it's like when I got my braces off in high school, I became popular again and everybody started to rush towards me and become my friend. And I had to say, I can't accept that anymore.
So I put up my defenses so the baby puts up its defenses.
It raises its afterload.
So now you have a situation where less blood comes in. It's harder to get blood out because the body is saying I can't accept all this at one time.
And then we know that the heart has an intrinsic discontractability.
You so all of that leads to this acute cardio pulmonary Physiology where the baby's actually back up the blood into the lungs and get sicker after the procedure.
So we've come up with some novel ways to really mitigate this. Now it occurs less with device closure than ligation. But using medications to lower the resistance and help the heart contract like Mirinone giving post op sedation to decrease catecholamine release and optimizing the ventilatory support has really.
Been beneficial and these are things that you can think about as a group in managing these kids after the device closure.
So I'm gonna end.
Kind of with this, you know, device closure is feasible and safe.
I I would agree.
I think there's been a rapid adoption of device closure since 2019.
I think we're seeing an improvement in short term outcomes.
Less length of stay and lower mortality, I still think.
I think the jury is out on all of the adverse events and we're partaking in a randomized control trial now to really understand the impact, both short term and long term.
And my take home message for anybody out there is early referral and developing a robust kind of referral program with Doctor Heibel, Dr. Hernandez and all the other stakeholders here to really understand.
Where these babies coming and where they're going? And if you're a general pediatrician out in the community.

Community. You then have a point person to speak to in case you get that X-ray that I showed up in the beginning or there is some complication long term that that we haven't yet encountered. So we built our PDA program and basically we have institutional stakeholders we have.
Centers, we have a Qi registry that could be then utilized by all fellows and trainees to ask really great questions and we're involved in academic endeavors which we're 100% willing to partner with you guys to really grow this nationally.
We built a research program which is really novel.
It's focused that not only on the PDA, which again we're looking at two randomized kind of control trials trying to decide.
Is device better than conservative?
And then we're also doing a randomized control trial looking at the use of mirror known to mitigate some of the complications after we close it.
But what I'm really excited about is the work that we're doing with assessment of a lung function both before, during and after.
And I talked about this yesterday.
We're also doing neat, non invasive neurodevelopmental assessments before, during and after closure with nears and we're also really engaged at looking at some of the.
Follow up data. What are these babies look like? A two or three years of age and their neurodevelopmental testing. And then like all of you out there, we're trying to use AI to have some predictive analytic and measures to tell us who are the babies that need their.
PDA, clothes or who are the babies?
We should really just leave alone.
So I put this up here because I love this.
This is a paper from Brazil where they used a device closure.
To close the PDA and conjoined twins.
I'm not suggesting that these are the babies that you should be starting with to build a program, but the sky is the limit now that we have these techniques were able to save even the sickest babies that we didn't know had a problem out there. So my conc.
Is really that us as a community?
Pediatricians, neonatologists, cardiologists, nephrologists, neurologists, pulmonologists.
We need to be honest with families about the unknowns of PDA treatment.

And adoptive culture of research.
That supports development.
Here's a QR code with all of the references and all of our Boston PDA closure programs.
I'll leave the slide up here for a few minutes and I'm really thankful for the opportunity to really present this data over the last couple days and be with all of you here today.
And I'm happy to answer any questions. This is a bit moji of of me that my son made before I came.
He thinks that this is what I'm doing when I when I travel around and speak, but in reality.
I get to spend the time with all of you and I'm just thankful for that.
So thank you again for this opportunity and I'm happy to answer questions.

Kamat, Deepak M 53:10
Thank you, Doctor Liu, for that wonderful presentation on PDA. There is a question in the chat box.
I'm curious what is the price of Piccolo?

PL

Philip Levy 53:20
Wonderful question.
The price of piccolo. I think the device is around $10,000 and it's matched to what the the kind of a surgical procedure costs. When we did a cost analysis, you know initially we thought, oh, the price of doing device closure may be more expensive than doing.
A surgical ligation? It's actually the same. So there's no difference.
In cost and when I mean cost, I mean total hospital cost.
With the amount of echoes that you do the the the cost in the ICU, the Cath lab, there are different devices that exist out there and I don't know all the pricing for everything but but it's a wonderful question because I think when you're building a program and.
Doctor Haivell will speak more to this as she builds her program.
You have to really take into account cost, but I try to manage my babies without thinking about costs and I try just have this tool in the tool bag and provide the best care.

Kamat, Deepak M 54:18

Thank you.

Any other questions, comments.

You can ask questions directly to doctor Olivia, or you can put them in the chat box.

PL

Philip Levy 54:33

And I don't know.

I don't know if Doctor Heibel is on the call or not, but but I I really I would encourage those out in the Community, even the general pediatricians.

You know you're going to care for, for even children who have cardiac issues and you know, she's a wonderful provider with a long track history.

And and basically.

You know, in the chat, doctor Nanis also mentioned something about long term neurodevelopment.

So yeah, I I I think as.

Neonatologist, we try and fix problems to get rid of immediate issues, to make us feel better, but in reality we need to think about what are the issues that we're seeing in hand and how they're affecting the long term neurodevelopment. So in our in our registry we have.

157 babies who underwent device closure and basically we are able to now match those 157 with some of the New England follow up neurodevelopmental outcomes where babies come back into the clinics at.

Kind of two to three years of age and get extensive Bailey score testing to give us that outcome and I'm hopeful that what we see is that that these device closures are giving us an incremental improvement in neural developmental scores.

Now if it's the opposite, you know and we're finding that the scores are worse, then I really have to go back to my interventions and think about is the intervention we're doing the right thing? It feels like the right thing.

I think we're on the right path.

But I think to doctor Hernandez's point.

Point and working with you know, interventions like Doctor Hye, but we really need to focus on both the short and long term outcomes as you're building your registry and your programs. Excellent question.

Kamat, Deepak M 56:14
Thank you.
Any other questions, comments.

Philip Levy 56:32
Jim, Jim, little things that people have pointed out over the last couple days.
Transport of these babies.
Some data out there has shown that really the the impact of transporting babies into your hospital or even transporting babies from the NICU to the Cath lab has minimal to almost no effect on kind of their short term outcomes.
We have not seen that to be done.
We've also seen situations where babies have had this procedure done on both the high frequency oscillator, the jet ventilator, so in the past those were barriers.
Really, I really just highlight it.
It's a really collaborative effort between a neonatologist and and and the interventionalist and cardiac anesthesia and respiratory therapy to really provide this high level care and and I'll end you know I'll kind of end with this, you know neonatology, antenatal steroids, surfactor replacement therapy. We've gotten better at.
Mechanical ventilation and nutrition.
That I know your division chief is really focused on.
Those are the four tenets that have improved care.
For neonates, over the last 30 or 40 years, I think in 20 years we're going to look back on this intervention and I think this may be another tool in our tool bag that it improves the care of a select high risk patient population. And I just really.
Want to thank everybody for the opportunity to be here today.
It's just been wonderful to spend time in San Antonio with all of you and please reach out to Doctor Hernandez or Doctor Haibel or myself with any questions about this procedure related to the PDA.

Kamat, Deepak M 58:03
Thank you, Doctor Levy.
Thank you all for attending this morning, Jenn Brown, I'm going to conclude.
Have a wonderful Friday.

We'll see you again next Friday at 7:30 AM Pacific.
We appreciate it.
Thank you.

PL **Philip Levy** 58:14
Thank you.
Have a great day.

Kamat, Deepak M stopped transcription