Navigating the Frontiers in Management of Severe BPD -Pediatric Grand Rounds-10-11-24

Pediatric Grand Rounds-20241011_072914-Meeting Recording

October 11, 2024, 12:29PM

59m 33s

Calderon, Delia started transcription

Ranch, Daniel 0:51

Good morning, everybody.
It's 7:30, so we're going to get started. And actually, Doctor Shadai, can you minimize that team screen?
I'm not sure why it keeps popping up for you.
There we go. Great.
And you can unmute your mic so you'll be ready to speak.
But good morning everybody and welcome to pediatric grand rounds.
Thank you for attending. As a reminder, please meet your devices as you log in.
Questions will be safe for the end and the participation code will be placed in the chat period.
But let's give a warm welcome to Doctor Rupa Sidhah, who is currently an associate professor of Pediatrics in the Division of Pediatric pulmonology, cystic fibrosis and Sleep Medicine.
And she's the director of the severe BPD multidisciplinary at Penn State Health Children's Hospital. Doctor Sudhai started her research and clinical career at Penn State Health Hershey Medical Center soon after her fellowship.
And since then, she has focused her interest on extreme preterm infants with severe lung disease and pulmonary hypertension.
She is the founder and director of the BPD Multidisciplinary program to provide comprehensive inpatient and outpatient care.
She is also the site director for the BPD Collaborative and International Collaborative of Centers geared to improve quality of care for infants with severe bpd to further care for these preterm infants and their outcomes, she is invested in translational research to identify noninvasive biomarkers for early identification of.

Infants Dr. Sudhai has received multiple awards, including the Eunice Candy Schwieber National Suit of Child Health and Human Development research Career Development Award and the 2022 Pulmonary Hypertension Association. Early career mentoring scientist award.
So, ladies and gentlemen, please welcome doctor Sudhai.

Calderon, Delia 2:39
Thank you very much for the kind introduction, Dr. Ranch and good morning everyone.
Thank you for joining me today and especially want to thank you, Doctor Sagner, for inviting me to give the talk and the opportunity to be here.
So today we are going to.
Talk a little bit about management of severe bpd and some newer guidelines and approach.
Have no financial disclosures.
Our learning objective for today would be to review different clinical phenotypes of patients with BPD and to discuss management of established severe BPD and to understand the role of multidisciplinary care in children with severe bpd.
As we are all aware, with the recent advance in neonatal care, there is improved survival of extremely premature babies.
And this has led to increased complications such as bronchopulmonary dysplasia or chronic lung disease, of prematurity, and also one of the more severe complications, known as pulmonary hypertension.
So as you're all aware, during our embryologic phase, we have the around 24 to 26 weeks is our canalicular to saccular phase transition and babies born at this gestational age do not have a fully developed or matured terminal bronchioles or alveoli.
And when Doctor Northway?
Defined BPD back in 1967.
He described this as a chronic lung disease of premature infants with progressive emphysema and fibrosis associated with mechanical ventilation and oxidative stress.
And at that time the patient population that were born were relatively later on, like around 3432 to 34 weeks of gestation. But.
As we saw much younger.
Babies who started surviving, especially with the surfactant use, there was a revision

to this where.
Alan Jobe defined this in 1998 as infants who were born between 23 to 26 weeks of gestation, had arrested long vascular and alveolar growth.
So there was a transition from fibrosis and antisemitis changes to more of arrested growth of the alveoli and the blood vessels.
In 2001, this is the most commonly used BPD definition, where Alan Jobe and Bangkalari classified this into mild, moderate and severe bpd, which I'm not going to go into detail since you're all pretty familiar with this. However, this definition has seen many.
Many more attempt at revising. This definition has gone on and the most recent one we have.
Is from 2019.
By Jensen et al, where they described any respiratory support at 36 weeks irrespective of prior duration or current level of oxygen therapy.
Was then categorized into grade one if they needed any oxygen flow through nasal cannula, but less than 22 litres per minute and grade 2 nasal cannula at flow rates greater than two litres per minute per minute.
Are invasive, positive pressure ventilation or non invasive and then grade 3 as invasive mechanical ventilation?
So they have been many different definitions, but we still have significant limitation because.
These definitions are defined by the therapy.
So based on what we are managing these patients with, but not necessarily based on the underlying pathophysiology.
And also what is happening is we are pulling all the premature babies at one time point for the sake of the definition at 36 weeks.
So we are taking the babies who are born at 32 weeks and also babies who are born at 23 weeks and piling them all in one under one umbrella.
While the pathophysiology can be very different between these babies, based on the management and also there is variable lung Physiology.
So we definitely need a more robust way of defining bpd.
Nationally, incidence of BPD is variable.
However, it's usually reported around 16% in those less than 32 weeks of gestation, but those who are born at less than 28 it can go up to 40 to 45%, approximately around 50,015 thousand new patients.

Develop BPD in United States annually and close to 2000 infants.
Have severe bpd and need mechanical ventilation at home.
The pathophysiology is highly complex because there are factors that are that can affect development of PPD and then perinatal factors.
Fetal you know, prior to conception are you know soon after conception pregnancy abnormalities and exposure of fetal to antenatal factors.
Can modulate development of PPD and soon after birth.
There is injury in the initial phase when there is acute injury followed by repair that can also predispose to development of BPD and over the time what we start defining as BPD around 36 weeks is when we start noticing the healing and remodeling phase of this L.
Development.
So.
In a nutshell, we have multiple factors intra Tor and growth restriction Antonio factor such as choreo, amnionis.
Metronome, hypertension, genetic and epigenetic factors.
Nutritional post Natal nutritional impairment PDA, oxygen toxicity ventilator induced lung injury and post Natal infection.
All of which?
Can lead to one big umbrella we call BPD, which again can have different phenotypes based on what are the drivers.
For this pathology.
When we talk about BPD, we spoke about what Doctor Northway had described earlier on, where there was significant lung injury with parenchyma fibrosis due to mechanical ventilation and oxygen toxicity and then.
Then we have a newer definition now with improved modes of ventilation and increased use of surfactant use.
Where we have arrested growth, we don't have so much inflammatory changes, but we have simplified alveoli and also.
Sparse pulmonary vascular development.
Does it mean we don't see the fibrotic changes and cystic changes that was described as old bpd?
Not necessarily.
We still continue to see the fibrotic changes in extremely severe BPD where we have a combination.

Of alveolar simplification and delayed vascular growth combined with areas of fibrosis and cystic changes.
And they can also have pretty significant pulmonary vascular disease on top of small and large airway injury.
So this is a schema to again.
Highlight the development of.
The alveoli and pulmonary vasculature in the premature infants.
A new BPD where there are simplified alveoli and also blood vessels and in this image we can see what we call pruning of the pulmonary vasculature.
Where we don't have as many vascular structures as you would see in the normal infant. And this is again a 3D reconstruction of the pulmonary vasculature, highlighting the pruning.
Catherine Wu.
Et All from Chop did this very good study looking at the clinical to define clinical phenotypes of severe bpd.
So they did.
On a cohort of severe BPD patient they did CT scans, they performed bronchoscopy and also cardiac catheterization, and 1/3 of these patients with severe bpd had a significant overlap. Of all these three.
Phenotypes and as you can see in this particular population they were like half of them, over half of 50% of them had pulmonary vascular disease too.
The clinical features of BPD is variable.
Mostly they do present with hypoxemia tachypnea. They have increased work of breathing, but they can also present with just poor growth.
When we talk about evaluation while clinical features is the way to diagnose, sometimes looking at the blood gas which shows hypoxia, hypocarbia, and respiratory acidosis can also be the hallmark, especially in acute pulmonary exacerbation of PPD.
Chest X-rays can show hyperventilation or hyperventilation.
Areas of electrics is also migratory, atelectasis and sometimes pulmonary edema and pie.
And here I have two X-rays of very different appearing BP DS on the right hand side.
We have more cystic and fibrotic, what we classify as more severe.
Bpd changes are on the on the right hand side is an X-ray of a patient.
The more milder disease or more simplified disease where we don't see as much

fibrosis, but it is consistent with alveolar and pulmonary vascular simplification.
In some cases, a CT scan would be warranted, especially if there is suspicion for sifactin protein deficiency, or if there is concern for interstitial lung disease associated with BPD.
And we notice that.
The CT scan has much more granular information compared to what a chest X-ray can show us, even in terms of the severity of the lung disease in itself.
So that can be helpful. Sometimes bronchoscopy would be helpful to.
Evaluate for airway disease, which we will talk about in a few minutes.
And echocardiogram helps us.
In screening for a pulmonary vascular pathology and if there is a concern for aspiration, swallow evaluation would be.
Important.
So moving on to management of BPD, the five main strategies is to avoid infections.
To avoid pulmonary hypertensive crisis and optimizing growth, which is the most important of those and provide intensive developmental care while minimizing the impact of the respiratory support.
When we talk about the large air with disease, because of the significant, the traction and stress that the Airways go through while the Airways are not fully developed and the cartilage is not matured enough, they are at high risk for developing trache Malaysia and also.
Broncho Malaysia when there is any incidence of airway manipulation such as intubation or prolonged recurrent recurrent intubation.
They're also at risk for developing sub GLA dot stenosis, or tracheal stenosis.
We often sometimes see granulomas developing at the cords or in the Subglottic region, and sometimes this picture can be.
Confounded with.
A coincidence of complete cartilage tracheal rings or tracheal, esophageal fistulum.
Management of typical Malaysia is through manipulation of the peep, which is more common.
In very severe instances, he and in distal airway Malaysia helium oxygen mixtures have been used and some centers do perform iotopaxi with significant tracheo Malaysia.
For specific surgical correction.
But this is not commonly performed in this age group.

Small airway disease.
Which microscopically do present with thickened epithelium and hypertrophy of the smooth muscles in the small Airways.
Sometimes these can respond to bronchodilators, however.
There is a genetic variability in response and this is not a routine use of bronchodilators.
An inhaled and systemic steroid.
Again, these are not routinely recommended. There is no.
Evidence that shows routine use of these medications help.
In either prevention of BPD or progression of BPD, however, studies have shown that.
Short term use of the systemic steroids have been helpful in pulmonary, during pulmonary exacerbations and similarly with the bronchodilators too. They have been shown to improve.
Long compliance during short periods of this use.
Mucolytics such as Dornier's Alpha has been used very occasionally when the concern has been very thick. Secretions that are not typically cleared using the bronchodilators.
Then we have the parenchyma lung disease, which is often what we refer to when we look at the chest X-rays.
Some of the medications that are used and shown to be effective are furosemide, thiazides and aspirinolactone. However, routine use is not recommended, but during when there is evidence of pulmonary edema or.
Low compliance of lung during ventilation.
Of these, diabetics have shown to improve the lung mechanics.
But more importantly, in lung parenchymal disease, it is a ventilatory strategies that would be helpful.
While we do use.
For preventing BPD, very gentle ventilatory strategies such as.
Low tidal volumes we have around 4:00 to 6:00 ml per kilo.
Short inspiratory time.
We use gentle peep as needed for long recruitment and the goal is to achieve the lowest Fio 2 possible.
We also aim for oxygen saturations between 88 to 92% and providing permissive hypercammia.
Which works great, while in the earlier period. But when we look at the.

Pathology of more severe BPD, where we see heterogeneous lung disease.
As we see in this picture, we have alveoli that are at a lactatic that have high resistance and low compliance and then we have.
Few normal alveoli or you know areas of lungs which have normal compliance and normal resistance and then we have a few more.
Where?
Areas with high compliance and low resistance, which seems to be the over distended the hyperdense areas that we see on the X-rays.
So when we use the low tidal volume and the gentle ventilation strategies, most of the ventilated.
Guests enters those areas that have high compliance and low resistance and hence.
It it fails to recruit the at electric part of the lungs.
And this leads to regional over distension and more Dead Space resulting in high pco two and also need for higher Fio 2 because of VQ mismatch.
So in these instances, having a strategy with higher tidal volume and lower inspiratory rate and.
You know, optimal eye times will give enough time for the ventilated gas to.
Open U, those arts of electric or high resistant low compliance lungs because of the slow rate that goes with this mode of ventilation leading to optimal gas distribution and less adelect tests.
So the recommendation is to use larger tidal volumes anyway. Between 11:50 mill longer I time, typically around .6 seconds or longer.
And there is, if there's evidence of airway obstruction using slower rates for better mting.
So there is no air stacking and hyperinflation and manipulation of the peep.
Now this is a more complex.
Issue, especially if there is evidence of trachea Malaysia like how do we optimize the the peep?
There are various ways, either through direct visualization under bronchoscopy.
There are some centers that have used dynamic CT scan to see what's the optimal peep in these scenarios.
Or something. What we are doing in our center is.
We do do optimization study based on the ventilatory.
The flow volumes on the ventilate on the ventilators.
So here in the ones there is an established BPD. We also recommend targeting

oxygen saturations from 92 to 95%, moving away from the lower saturations which can further stress the pulmonary vasculature.
And higher PCO two are associated with worse disease outcomes.
So that is also we are moving away from this permissive hypercamia.
And then comes the topic of tracheostomy as to when is this indicated? So once we have patients stabilized with severe bpd on the the late BPD ventilator settings, if there is consistent need for or sustained need for mechanical ventilation with high support which are which we are UN.
To.
Be in. That would be an indication for starting this discussion.
Of tracheostomy in the in the group and the family and also if the patients are needing prolonged intubation, resulting in distress or spells.
That's another indicator that they might need a tracheostomy would be helpful.
And tracheostomy in the setting of prolonged abation would also help promote growth and developmental outcome.
So that the pay be can then participate more in the in occupational and physiotherapies.
But obviously this is a complex and difficult decision and needs a multidisciplinary approach.
Especially in this era where nationwide is a big shortage and we experience in harshitoo where although we do go the route of the tracheostomy.
Aim to get our patients home earlier on.
We have a big shortage of home nursing, so that kind of restricts the patient staying in the hospital longer, sometimes even needing their ventilator ventilation and coming off of the ventilator support while they are still in the hospital.
So it's certainly a complex.
Complex decision.
So pulmonary hypertension or pulmonary vascular disease associated with BPD.
It's more prevalent when the babies are much have a lower gestational age compared to those that are.
That are born later on and this incidence can vary anyway from 25 to 40%.
And.
Market pH in those less than three months of age is associated with pretty significant mortality, up to 40%.
Within the first two years of life, and if there is severe pH, this mortality can go up to

70% of this patient population.
And something else that can worsen the comorbidities that can worsen BPD or pulmonary hypertension or swallow dysfunction.
GE reflux oral secretions if there's.
Evidence of aspiration?
And, you know, increase upper airway secretions and they can present with.
In Tekitnia or frequent desaturations hypercarbia of poor weight gain.
Especially because this is not an aspiration event at one time and then the patient deteriorates, which also happens like we see in our neonatal ICU, but those with small amounts of micro aspiration.
Present with chronic symptoms such as achypnea's and frequent desats and poor weight gain rather than one single episode of decompensation.
The challenge with this is that diagnostic techniques lack sensitivities and spasticities, and often we need to we might need to repeat the studies.
In very severe cases of aspiration and reflux, G tubes, with or without Nissan's fund application might be warranted. However, in our institutions we have completely moved away from Nissan's fund application and in very severe reflux and aspiration risk we have.
Often go on the route of the GJ tubes.
Anti reflux medications such as H2 blockers and Ppis have been used and in very severe cases gastric repulsive agents or post pyloric feeds have been implemented.
As you're all aware, nutrition is the key in terms of managing bpd because of their hyper metabolic state, increased work of breathing.
Growth suppression from chronic stress and inflammation, and if they are on chronic steroid or diuretic use, this becomes much more of a priority.
While monitoring the nutrition, it's important to note just look at the weight.
Look at the linear growth.
For the for the overall somatic.
Performance of these patients, typically the calorie grow.
Calorie target is around 130 kilocal per kilo per day and.
We might need to increase this based on the.
Based on the patient's need, protein needs protein needs.
Ranges from 3.5 to 4.2g per kilo per day, along with all the other micronutrients need to be assessed on a regular basis.
Which is where given the complexity.

There is need for diverse expertise.
There is also a need for a focus group of providers who are familiar with the most updated literature since.
This is continuously.
Evolving field.
And often it needs commitment to the care of this unique and challenging patient population especially.
From the nursing standpoint?
There is a need for standardization of practice where there is.
No frequent change from one week to the next in terms of.
The practice managing these patients is concerned and continuity of care with the sub specialties from transitioning from inpatient to outpatient is key for successful outcomes.
This is our multidisciplinary team at our institution, so we have.
We have pulmonology, cardiology, neonatology.
We have respiratory therapists.
We have the NICU nurse managers.
We have home, ventilator nurse practitioner.
We have pediatric radiologist and we do round with our nutritionist speech therapist.
And E&T sub specialty once in two weeks to maintain the consistent core group along with the on service team to discuss our patients and most importantly, we also have our families as part of our working group.
So especially those with severe bpd needing tracheostomy, it is important to identify the outpatient once they get ready to discharge. I identify the outpatient primary care physicians, pulmonologist, cardiologist, and have a seamless transition from inpatient to outpatient.
For those who are not on a even on a ventilator, but also those on.
Like low flow nasal cannula, cannula, or aim is.
To prevent significant changes few weeks before they get discharged to maintain stability.
So there is no winning on their oxygen or two feeds.
Right before they get discharged home and also to monitor for consistent weight gain, we often have a hand off to the PCP by a phone call.
So there is a direct communication with the out patients of his team.
And we do emphasize on growth.

Monitoring weight and length percentiles and optimizing calories and also screen for comorbidities, especially in the setting of aspiration.
Early intervention referrals to monitor the neurodevelopmental outcomes is recommended, and all the patients get it mandatory.
That is infection precaution.
We recommend seasonal RSV vaccination until they are two years of age and then the annual flu shot.
And referral to pulmonology.
We recommend if there are infants with any degree of BPD, especially those who need home oxygen, are on inhalers or on the diuretics.
We do try to standardize our care in terms of how we wean outpatient supplemental oxygen in our BPD group.
These babies are assessed in the follow up clinic every two to four weeks.
We do have continuous pulse ox monitors on them until they are completely off of the supplemental oxygen. We do stepwise weaning of their oxygen and 1st we try to wean their.
During the daytime or during awake periods before we do the nighttime weaning and there if there is any significant history of pulmonary hypertension, we would like to do.
An overnight sleep study where possible or pulse oximeter study before we completely discontinue.
The oxygen at night time and even after discontinuing while they are on room air.
At least if they are closer to the winter months, we keep it through the winter months to use as needed for acute viral infections.
So the long term outcome for these babies, you know, once they're off of oxygen, it doesn't necessarily mean they don't have bpd anymore.
This is a lifespan disease.
Studies have shown consistent.
Or persistent pathology into adulthood.
There are many studies looking at.
You know, school age children having obstructive lung disease and also sometimes restrictive or trapping with.
The synaptic lung growth and.
There was this one study from Australia where they did HSCT scan on a cohort of adults who were born premature and.

85% of them had inflessima test changes.
Almost all of them had some structural changes on their CT scan, but 84% of them had emphysema test changes on their CT scan, irrespective of whether they were symptomatic or not.
So this is something the information that I typically share with families.
There are also studies that show abnormal grass gas transfer on to LCO.
Other than just obstructive or restrictive airway diseases.
Umm.
Something else that we note in those adults who are born premature, there have been multiple studies, especially.
Led by Doctor Carraghous, where there is evidence of pulmonary vascular disease in adults who are born prematurely.
And this was driven by the number of days on the assisted ventilation in the absence of pH in the infancy and these patients, the adults were.
Over asymptomatic, but still the cardiac did show subclinical pH.
And two of them did have clinical pH.
So in summary.
Bpd is a growing condition with complex lung disease, with varied phenotype and high morbidity.
Focused clinical and research efforts are needed in management of BPD.
In conjunction with prevention of PPD, while there's been a lot of studies in preventing BPD, there is lack of that effort.
A need for increased effort in managing BPD as.
There is lack of evidence for a lot of these medications and management strategies need for identification of long term sequelae in this high risk group as they transition from childhood to the adulthood.
Because this is not just restricted to early childhood, this is a lifelong pathology.
So how do we?
How do we strategize for these patients to be followed closely even after their transition into the adult?
Do we need a separate BPD clinic?
For these patients, just like the, you know, the cancer Survivor Clinic, do we need a BPD clinic that needs to span the life?
The lifetime for these patients for early identification of adult onset clinical symptoms.

So with that, I'd like to thank you all for your time and I can take any questions that you have.

Ranch, Daniel 38:33

Thank you very much for that wonderful presentation.
If you have a question, please go ahead, raise your hand or unmute yourself.
We can also place questions in the chat.
S doctor seidner seidner.

Seidner, Steven R 38:49

Thank the sedaya. That was wonderful.
One question I have is, you know, and I know some of your research is looking forward.
How do you see us predicting those that weren't obvious at the end of their neonatal course but are still at high risk for adult pulmonary vascular disease?
What kind of predictors do you think we'll have in five to 10 years?

Calderon, Delia 39:14

Great question.
Right now, based on the previous studies, clinical studies, some of the predictors have been the number of days on the ventilator.
That these patients have been while in the NICU.
But we need more robust.
Clinical parameters that can help us predict.
Some of the you know, there's been a lot of work in terms of.
You know Endo typing these patients, you know, my particular research area is looking at the micro RNAs that can predict development of vascular disease at least in the early childhood.
But that is a potential for looking at the long term into adult.
Adult patients because there seems to be.
A multitude of you know when we look at the pathophysiology.
You have antonidal factors that can predispose to that, and we have perinatal and also we don't have much information what happens.
What drives this vascular disease later on in life with PPD, right?
Because they're already at high risk.

But how does the, say, viral infections modulate this risk?
How does exposure to secret smoke modulate districts?
So it's a very complex pathology and I think there's a, there's a very big need.
For.
These patients.
And one way to do that is by.
Establishing a pathway where we can follow these patients on a regular basis and collect all the data, build a database that can help us, then study.
What are the drivers of?
What are the predictors of developing?
Adult pulmonary vascular disease.

Ranch, Daniel 41:12
Doctor Gong, go ahead.

AG

Alice Gong 41:14
Well, thank you.
Thank you for that presentation.
The Swedish studies on long term follow up have shown that babies who are diagnosed with bpd tend to die earlier, and they also have a lot of heart disease.
Which you know, so we don't know what the cause is.
It's probably the BPD and put me in hypertension.
The challenge I see is that we have babies that we follow up to five years here.
And once the babies are off oxygen, the parents tend to not want to go back to the pulmonary clinics for follow up.
And they tend to miss those appointments. And so I think that.
That the feeling is once they're off oxygen, they're fine.
Which drives me nuts, but I think that we need to understand these kids on a long term basis and that they do need periodic evaluations.
Because they do die much younger and we have to figure that piece out. And so I applaud you for the work you're doing. And 'cause, we need to know that information.
Thank you very much.

Calderon, Delia 42:30

Yeah. Thank you.
Thank you for the for the comments.
That that is a challenge.
That is a challenge.
Change how do we educate our families and?
You know, emphasized the importance of this long term follow up.
So we start with that education right at the get go. When we start seeing them in the NICU. Even when I see the patients like the first time, I see them outpatient, my visits are sometimes an hour long just because we spend so much time educating and that.
Like you said, once they are off of oxygen, everything seems like OK.
We don't, really.
You know the kid has.
And not just the parents, right?
There are so many even primary care there is.
We need more education to say, hey, this is not just an early childhood condition. We need long term follow-ups and.
Even when they've been off of oxygen, we try to, you know, do the same education.
And that is one thing that we have started as part of a BPD program is to follow them through the until the adulthood.
I still don't have anything.
Hopefully we'll have, you know, an adult pulmonologist who would be interested in BPD.
But I think we need that pathway set in there.
We can follow them, even if not every year, at least every two to three years.
So one thing that I tell the parents is we need to look at their lung function.
So I need to see them at five years of age and then we again follow them at, you know, three years after that at 8 years and then at 10 years.
Where we try to collect all the data in.
Of their lung function, one to follow the patients, but also to build our database and collect the data point so we can educate ourselves going forward.
How can we better define these phenotypes? And you know what kind of like restrictive lung disease are they having obstructive pattern? Do they have airway reactivity?
We don't have enough data to see what's upset of these patients.

Develop these different phenotypes so there is.
Definitely that lack of information and I we do talk about early death in this patient population, which you know, what is the parents. But I hope that also highlights the importance why we stress so much about this continued follow up and you know we talk about annual flu.
Shot, you know.
Eliminating smoke exposure in these patients.
But I think there's a lot that needs to be done, and I think there's also more data.
For the early death and cardiac disease cardiovascular diseases, higher incidence of cardiovascular is.
There's some evidence of high risk for these.
Premature babies for metabolic syndrome, right?
I mean, they have at high risk for cholesterol abnormalities or hypercholesterolemia.
There are high risk for obesity, diabetes, so they have this high risk for metabolic syndrome, which probably is due to some modulation of growth factors.
In this population, given their prematurity and early stress exposure, but there's not much information or data there either.
So I think this you know as we see more and more premature infants who are now surviving into adulthood, we need more.
More robust efforts to study these patients and maintain that long term data collection.

Ranch, Daniel 46:28
There's a question in the chat, then I'll go to Doctor Mckernan, then Dr. Marrera, Dr. Wu, one of our Intensivists asked. How does your group help prepare caretakers of babies who are going home with trachostomies and their care and how to deal with emergencies.

Calderon, Delia 46:45
Thank you.
Great question.
We are very fortunate to have a very robust homeland program.
So.
This helps with our BPD program because we start seeing these patients at around 36 weeks.

With any kind of respiratory support, that's when we start seeing. Now when we see those with severe bpd, those on mechanical invasive mechanical ventilation, we see them more regularly.
And we start having this when we start having the discussion of tracheostomy.
We have our home practitioner be part of that, so we set up a relationship right from the get go and once and then we collaborate with our ENT who does the surgery and we work together. Once they agree for the tracheasomy, we have a six weeks training program.
For these tracent patients.
Where we need at least two care providers. You know, being able to.
So take care of the patient while we also look and you know, we need to have nursing at home, but we need at least two care providers who are adapt at.
Taking care of these babies, we have similar training to for addressing barriers, emergency situations at home.
And once they discharge home.
So we have like.
Medical home, like setting so our.
Home owners practitioner is.
A key person.
Where all these home and patients with any concerns they are reaching out and we have another nurse practitioner who calls them within two to three days of being discharged home to kind of, you know, troubleshoot anything, any concerns they have. We also have within a month of them.
Discharging home. We see them in the clinic as well, and then we do a lot of telehealth visits with these patients.
Who have issues with access?
But we've had a very robust program, which is now almost 20 years old and we are very fortunate to have a core group of providers that help run this program.

Ranch, Daniel 49:10
Doctor Mckernan.

M

McCurnin 49:12
Yeah. Thank you again for a wonderful presentation and back to pulmonary hypertension. As you know, it's a determinant of long term outcomes and mortality.

And you mentioned how you wean the oxygen carefully.
Particularly in the presence of pulmonary hypertension.
But I'm wondering, do you use other agents outpatient to manage your pulmonary hypertension like bosin tan or sildenafil?
And if so, how do you coordinate?
Weaning those agents.
As well, on an outpatient basis.

Calderon, Delia 49:50
Thank you.
Excellent question again.
I'm very blessed.
I should say I have this excellent cardiologist that I when I started developing the program and I reached out to him.
He's he's also director of the pulmonary hypertension program and he.
We work very closely together.
So if there is a significant pulmonary hypertension, so the first line of management, I know that's another topic in itself.
Is to optimize the respirator support right in the pulmonary hypertension associated with PPD and in spite of that, they continue to have signs of vascular disease in conjunction with the cardiologist. We do start them on sildenafil.
I mean, obviously ruling out other things such as you know on the echocardiogram, if possible, you know, rule out pulmonary vein stenosis. And if they have like a significant hemodynamically significant shunt such as pdra ASD that needs to be addressed.
But if the patients are going home on the pulmonary vasodilators.
Then, or even if they don't need pulmonary vasodilator, but they have signs of pH.
Mild pH.
We see them.
We have a combined clinic, a multidisciplinary clinic where we see those patients together.
So we literally sit together.
We review the echocardiograms together.
We review how their growth, how their oxygen requirement is. So we try to.
We don't, once the pulmonary hypertension is well controlled on the

echocardiogram, we try to wean their oxygen first, not necessarily the vasodilators to make sure they tolerate weaning the oxygen, since that is one of the pharmacotherapy for pulmonary hypertension and we gradually wean the sildenafil if the patient.
Has been stable for a number of months.
Off of the respirator support.
So that is what we do and it is usually a combined effort between me and my colleague, the cardiologist. And this also includes the diuretics. If they are on diuretics, we do very slowly in those patients.
Now when it comes to.
Bosantin or the 2nd pulmonary vasodilatos. Typically Ifill is not enough and then the pulmonary hypertension is not well controlled.
That's when we recommend a cardiac catheterization. So we obtain a cardiac catheterization to better delineate the vasoactivity, you know, rule out other abnormalities such as pulmonary vein stenosis.
Before we start business and typically these kids, when they're sick enough, they're in the ICU and that is where we do the percenting typically in the pic you not as much in the neonatal ICU.
So they go home on that and again the weaning process is very slow and you know mostly driven by my our cardiologist.
But we we work very closely together. You know, if we are not able to see the patient in together for whatever reason, we are constantly texting and discussing, OK?
Should we do this?
You know, so there is.
It is a combined effort.

M **McCurnin** 53:24
Thank you for that answer and thank you for pointing out pulmonary veinsonosis is a long term issue as well.
That's sometimes neonatologists aren't cognizant of that concern.
And it can be hard to identify and but it can present in the in the NICU early on before they go home.
So I think always being vigilant for the concerns about pulmonary vein stenosis is really important.
Thank you for pointing that out.

Calderon, Delia 53:50
Yeah. Thank you.

Ranch, Daniel 53:53
Doctor marrera.

Moreira, Alvaro G 53:56
Hey, can you guys hear me?

Calderon, Delia 53:58
Yes.

Moreira, Alvaro G 53:58
OK.
Great, rupa.
Thank you so much for the great work that you do.
Very excited and interested in in a lot of lines of just a clinical as well as some of the investigations that you're conducting. And so I have, I have a two prong question. I'm more interested in some of the bioinformatic work that you're currently focused on and can.
You tell me the first question is can you tell me how?
You are currently using some of that Micra RNA profiles to help potentially differentiate between those various phenotypes of BPD.
Specifically, are you are you obtaining blood samples?
When are you obtaining them?
Or are these tracheal samples from that first week of life? And then secondly, are there specific signaling pathways that you think micro RNAs are helping regulate right now that are critical in the in the in the lung development of these preterm infants?

Calderon, Delia 54:53
Yeah. Thank you. Excellent questions.
Actually prepare slides for those two for the research part of it, but I'm excited to talk about it.

So when I started our work, you know it was driven by, you know, I didn't start as a as a as a researcher, but as a clinician. During my P consoles. Notice how challenging it was to diagnose pH in this patient population. And my goal was to.
Start looking at non invasive biomarkers that can help delineate these babies with pulmonary hypertension from those who have bpd cause the symptoms overlap between the two, right.
So it's kind of hard to tell who has pH and who don't.
And while we do the echocardiogram, it is no sometimes you don't get a good, good window.
And sometimes, if you don't specifically ask for.
PH patameters.
They're not even mentioned right in the report or, you know, the talk about OK good ventricular function. But I'm not looking for that.
I wanna know what the interventricular septum is doing.
I wanna know what the.
You know TRV is. So we don't get all that granular information.
So my goal was to look at a non invasive marker and that and that time we started looking at the tracheal asperates.
So we did a multi omic.
We did proteomics.
We did microorn as we did.
Transcriptomics you know, mrnas in the tracheal aspirate to identify.
So we compare 2 cohorts, those with BPD, those with BPD and pH, to see what delineated between the two phenotypes.
So pulmonary vascular disease and without pulmonary vascular disease in the setting of the BPD and we identified.
Marcus, which when we did the in silico predictive modelling, the downstream targets were.
Insulin and particularly we were more focused on the microdronase 'cause. They are the gene regulators.
And modulated the you know the mRNA translation phase.
So when we focused on these micro RNAs, we had pathways that.
Were targeting PDG FA and your protein like protein 4.
And at Andf Alpha, among some of those markers.
So.

Now we are looking more in depth into the mechanistic pathways of these microorganis and in particular mid 29 a it has been of interest that seems to be. Upregulating some of these PDGF, the vascular growth factors, are actually down regulating the vascular growth factors in the pulmonary artery smooth muscle cells. Umm. And I'll be excited to share that information this afternoon.

Moreira, Alvaro G 58:04
Looking forward to hearing more about that.

Calderon, Delia 58:08
Thank you.

Ranch, Daniel 58:16
Any additional questions?
Doctor Cider did comment that Doctor said.
I will be discussing research at 11 O clock as well in the pediatric conference room.
Allow an awkward 10 second.
Any more questions come up.
Well, if there are no more questions.
Thank you again, Doctor Sudhai, for that wonderful presentation.
And have a safe journey home.

Calderon, Delia 58:57
Thank you.
Thank you for having me.

Sheila Reifle stopped transcription