

[MUSIC PLAYING]

CAREN S. GOLDBERG: Thanks to the committee who put this together. It's really an honor to be here. I have nothing to disclose except to say it's incredibly humbling to speak after Jenna and Brad all the time. And Terri, your talk, thank you so much. It was so compelling and inspiring, and I think we all learned a great deal. So I'm humbled to be able to speak in the same session.

So what I get to talk about is, what can we do to improve neurodevelopmental outcomes for our patients? And just to give a preview of what I'm going to talk about, I want to review, how did we get to the point that neurodevelopment can be emphasized? How do we get to think about it at this time? Overview of what we know about neurodevelopmental health outcomes with going over just a small selection of the studies that have been done to show us where we are with neurodevelopmental outcomes for our patients and some of the work that's been done on interventions.

As Brad said, I'm going to review portions of the American Heart Association statement and recommendations for us in cardiology. And then, I want to talk about the importance of partnerships and collaborations in optimizing neurodevelopmental outcomes.

So flash back to when I was a fellow, it was when we were first reaching-- well, when I became conscious, I guess, of reaching improved survival. And it was right during my fellowship that Dr. Bove and Dr. Lloyd published our improved survival for patients at normal risk at five years was up to 70%. And this was huge. In fact, a few years later, the group from Children's Hospital of Philadelphia showed improved survival over eras-- and again, about 70% in the mid '90s of patients with hypoplastic left heart syndrome, compared to 30% just a decade prior.

Now, most recently, the group from Children's Hospital of Philadelphia has also shown improved survival following the Fontan operation. And so these are all patients who, regardless of their single ventricle abnormality, underwent a Fontan. And in this most recent era, 2003 to 2009, survival is at 95% compared to, again, about a decade earlier was only 85%.

And one more look at the changing profile and demographic of patients with congenital heart disease, broadening to all patients with congenital heart disease. Paul Khairy and colleagues looked at the age of mortality from two time periods for people in Quebec who had congenital heart disease. And the bar graph on the left demonstrates the age of death for all patients with congenital heart disease who died between '87 and '88, and the graph on the right shows the age of death for those who died between 2004 and 2005. And this shows that, in the earlier era, more patients were dying during infancy, as compared to the later era, 2004-2005, when many patients with congenital heart disease were living well into adulthood.

And actually, this black line represents the general population of patients with congenital heart disease in Quebec during that same era. So quite impressive change in demographics. People with congenital heart disease, thankfully, are living to older ages.

So as survival has improved, morbidities have become more evident, and neurodevelopmental impairment is the most frequent morbidity in children with complex congenital heart disease. Humbling, right? As cardiologists and the cardiac area, the primary morbidity that we see relates to an area of neurodevelopment. It's about the brain. It's not about the heart.

I found this quote of Thomas Edison that I didn't know before. "The chief function of the body is to carry the brain around." And I guess, in our cardiology community, maybe we can think of it as a function of the heart is to supply blood flow to the brain.

So I wanted to go over, like I said, just a select few of studies that give us some sense of where we are in neurodevelopmental outcomes. So these are data from the single ventricle reconstruction extension study. In this study, in the original trial, patients were randomized-- patients with hypoplastic left heart syndrome and other single ventricles were randomized to have either Blalock-Taussig shunt or an RV-to-PA shunt at the time of their Norwood operation.

And we looked initially at neurodevelopmental outcomes at 14 months of age in those patients, and then patients have been followed over time. And this bar graph represents the follow-up at three years of age, when patients' parents completed the Ages and Stages Questionnaire. So about 200 patients from the single ventricle reconstruction studies' families completed this questionnaire. There are five domains on the Ages and Stages Questionnaire-- communication, gross motor, fine motor, problem solving, and personal social.

And that green line here represents where the bar would be in the general population, what percent of the patients would have an abnormal score on the Ages and Stages Questionnaire. And you can see, in the area such as fine motor skills, about a third of the patients had abnormal scores, and gross motor and problem solving was abnormal in about 25% of the patients.

This is looking, again, at patients with hypoplastic left heart syndrome at school age, and Bill Mahle and colleagues while at Children's Hospital of Philadelphia showed as others had that the curve is shifted to the left for IQ scores. But more importantly, in looking at learning and behavior, about a third of patients in their cohort were requiring special education, and about 70% had evidence of ADHD.

Looking at a different population, the group from Aachen, Germany, looked at patients who had transposition of the great arteries, who had neonatal arterial switch operations. And 55% of the patients had some type of neurologic, speech, or motor impairment.

And then, looking even more broadly at all patients with congenital heart disease, Matt Oster and colleagues, in North Carolina, they were able to look at their birth registry for all patients who had congenital heart disease and compare that to control students in the general population who did not have any birth defect. And by comparing scores on standardized tests at the third grade, they found that patients with congenital heart disease had a higher rate of failing reading, math, and even on both tests with an increased odds ratio of 1.2 to failing, both for those patients, for those people, who had some congenital heart disease.

So there is a risk. This is just a very small selection of the studies that have been done to measure neurodevelopmental outcomes. How about the fact that neurodevelopmental outcomes it has on quality of life? This is an interesting study, I think, from the Boston group where they asked parents of children with tetralogy of Fallot between ages 13 to 16 to complete the Child Health Questionnaire, which measures quality of life. A psychosocial health summary and physical health summary score come from that; the BRIEF, a measure of executive function, which Brad talked about; and the Connors, which looks at a measure of attention deficit.

And they found that, as your executive function was lower, if your score of executive function was lower, it had an impact on your psychosocial health. And not surprisingly, if you had attention deficit disorder, you also had a lower score of psychosocial health.

And so, when we think-- and I can't reach out into all these pieces, though we've heard about it in some of the other talks-- neurodevelopmental impairment has an influence on patient frustration and quality of life. It influences family stresses. And it ultimately has an impact on society as well if people are not able to reach their greatest potential.

So we have to think as a field, what are the factors that are associated with neurodevelopmental outcomes? What are the things that we can control? And there is more work being done looking at the intrauterine environment at this point, so more to come on that piece. Pre-operative presentation is a factor. Underlying genetic conditions, congenital structural brain abnormalities, socioeconomic status, perfusion methods, intraoperative techniques, post-operative complications, and long-term evaluations and interventions.

So of these factors, many of them actually are not modifiable, and some of the ones that are modifiable we've explored and haven't been able to find solutions. I'm going to talk about the few left over in red that we know a little bit about and then really emphasize what our long-term evaluations and interventions can help us with.

So Bill Mahle, again, when he was in Philadelphia, looked at the rate of neurologic events among patients with hypoplastic left heart syndrome. The neurologic of that was defined by seizure or coma, and there was an increased risk if you had a post-natal diagnosis. So if you didn't have a fetal diagnosis, the risk was higher of having a neurologic event.

This makes sense, right? Fetal diagnosis will reduce the preoperative risk of cardiogenic shock because know the patient's coming and instability. So it all makes sense, but this was the first study to really show that fetal diagnosis was valuable.

Dan Licht has demonstrated, and his group has demonstrated that patients with congenital heart disease have a less mature brain at any given gestational age compared to controls without congenital heart disease. And a follow-up study by David Goff and colleagues, also at CHOP, found that cognition, executive function, visual motor skills, and fine motor skills were reduced in those patients who were born prior to 39 or 40 weeks compared to those patients born at greater than 40 weeks. So the idea is to avoid preterm delivery if at all possible.

There are multiple modifiable factors that have been investigated in the intraoperative world, perfusion techniques of a variety of sorts. But really, there's been minimal return to date despite our efforts. The one thing that has been found to be helpful is the hematocrit at the time of initiation of bypass. So two trials from the Boston group were combined, one study of hematocrit of 20 versus 30 and another of hematocrit of 25 versus 35 at the time of initiation of bypass. And the group found that Psychomotor Development Index was better if you could at least get to the 23 to 25 range and still good up into the 30s.

So, with all of this investigation, these are some things that we can do, some things that we've learned, but we're left with thinking, OK, how else can we improve neurodevelopmental outcomes? And I would say that, after we've measured issues, it really led to the group of us led by Brad Marino and Bill Mahle to get together and think about what is it that we should be doing to improve neurodevelopmental outcomes. We have measured quite a bit. What can we do to move on?

One of the things that's central to this scientific statement is the understanding of the medical home, and it's important for us to recognize as pediatric cardiology providers that we may actually serve as the medical home for our patients. And so, the medical home is a team-based, family-centered, health care delivery model led by a health care provider to provide comprehensive and continuous medical care to patients with a goal to obtain maximal health outcomes. So it's not just about the heart. It's about making sure that the patient gets complete care. This obviously requires some collaboration, which we'll get to.

Because, as Brad alluded to, in our usual pediatric cardiology visit, we want to know how school's going, right? So we ask things like, so how's Joey doing? Is he ready to start school? And the parent answers, oh, he's very active. And we say, OK, great, or how is school going for Susie? She loves her teacher. Our response, excellent.

So what have we learned? Often, we don't really know much about school readiness or school performance by these regular questions that we ask. And when we hear the answers, we put it in the context of what our school experience was like, which is probably a lot different than what it is like for someone who's having challenges in school.

Instead, we could incorporate some simple questions into our clinic visit that might give us a little bit more information. We could ask the patient, tell me about your school day. We might hear a little bit more. What are you learning about in math? Can you tell me about yesterday's math lesson? Can you tell me a bit about your reading class? What books do you like?

How about for the parent, has Justin's teacher expressed any concern about any learning or behavioral issues? Does the teacher ever contact you? Has the school worked with you on an individualized education plan? These are questions that, if the child's not having any problems, the answers will be quick and it won't take much time. If the child's having some challenges, it will take a little bit of time, but it's probably well worth that.

It's recognized that not everyone will do that, though, and we have to think about who are the patients at high risk. And this is a schematic forwarded originally by Gil Wernovsky, and it's maybe one of the most oft-shown slides in talks related to neurodevelopmental outcomes in children with congenital heart disease. The graph doesn't actually represent data, but the concept that we all really believe-- that, with increased severity of congenital heart disease and the presence of a syndrome, we're likely to see an increased risk or increased problems with neurodevelopmental impairment that's likely to be more severe.

As Brad alluded to, it's not always all that straightforward. There are a lot of factors that play into this, but we think that we need to look at who is at high risk so that we know how to make our referrals.

So the group put together this list, and I think Janet showed it earlier. The people on the list are children who required infant cardiac surgery with cardiopulmonary bypass, children with cyanotic heart disease who have not required cardiac surgery but still cyanotic, and patients who have congenital heart disease of any sort associated with prematurity, developmental delay in infancy, suspected genetic abnormality, a history of need for ECMO or a ventricular assist device, the need for heart transplantation, CPR at any time, hospital length of stay more than two weeks, perioperative seizures, or significant abnormalities on neuroimaging or the presence of microcephaly.

The recommendation is that those patients who do not fit into that high-risk group, or those patients who are low risk, should be screened as per the usual AAP guidelines and refer if any concerns arise. For those patients at high risk, though, they should be referred for a developmental evaluation and monitored serially throughout childhood and adolescence with age-specific tools.

These are the current-- they change a little bit over time, I look at Erica, they change a little bit over time-- but the recommended times of evaluations. And the reason for these evaluations is, especially in the school-age group, they are generally at times of transition. So for instance, at eight years of age, you are going from learning to read to reading to learn.

It's important to recognize that we do have another role in our clinic setting as we think about our patients living more into adulthood in addition to the neurodevelopmental burden at young ages from instabilities and early operations the risk of increased atherosclerosis-- I have some, I guess- from acquired cardiovascular disease grows, and there is the issue with increase in cerebrovascular lesion burden on top of the early neurodevelopmental burden. And this schemata was put together by Ariane Marelli and I think is incredibly applicable and reminds us that it's so important that we provide healthy lifestyle counseling to our patients with congenital heart disease.

When figuring out how to take care of patients and their neurodevelopmental care, we can't do it alone in the world of pediatric cardiology. So it's incredibly important to identify interested and expert team members-- psychologists, neuropsychologists, and developmental pediatricians. And once you start to develop a program-- and talking about it just like in the inpatient world-- you'll find that there are a tremendous number of therapists, nurses, teachers. You'll hear later today from Brenda Henney, our school liaison pictured here, who has taught us a tremendous amount and has helped to do extraordinary work really in our clinic setting.

And it's important when thinking about development of a program to work with a center leadership. I think that John Charpie was a tremendous advocate for the development of our program, and it was incredibly helpful, and we wouldn't have been able to develop the program without John's backing.

And it's important to identify funding approaches. This could be the subject of a whole talk in and of itself, but it's important to think about what can be covered by insurance, where do we need philanthropic funds-- this is a big one-- as neurodevelopmental evaluation and care is expensive.

Another collaboration, as Brad talked about, is through the Cardiac Neurodevelopmental Outcomes Collaborative. The mission of the CNOC is to determine and implement best practices of neurodevelopmental services for individuals with pediatric and congenital heart disease through clinical, quality improvement, and research initiatives. This is actually a fantastic organization, not because of our involvement, but because of the involvement of so many and because it is this incredible multi-disciplinary collaboration. We all are learning from each other about what we can do to improve neurodevelopmental services and outcomes for our patients.

So I just want to summarize. So survival rates for even the most complex congenital heart disease have improved, and morbidities are now more evident. Neurodevelopmental impairments are the most common morbidity, affecting more than 50% of children with complex congenital heart disease. The pediatric cardiology specialist has an important role to play in improving neurodevelopmental outcomes for children with complex congenital heart disease.

Fetal diagnosis is helpful, and it's incredibly valuable to avoid preterm delivery whenever possible. In the clinic, we need to recognize the potential for neurodevelopmental impairments and ask questions to screen for these concerns. Identify those patients at high risk and refer for developmental and behavioral evaluations. And finally, really central to all of this is to build the collaborations to facilitate getting the needed evaluations and therapies for our patients.

So with that, I want to thank everyone for being here and thank our team for neurodevelopmental follow-up program.

[APPLAUSE]