

# PEDIAPOD NOVEMBER 2023 TRANSCRIPT

## **Geoff Marsh**

Hello and welcome to PediaPod for November 2023. This month, can illness severity scores be used to predict morbidity following pediatric sepsis?

Illness severity scores are commonly used for mortality prediction and risk stratification in pediatric critical care research. But as mortality has steadily declined in the pediatric intensive care unit, there has been increasing attention given to evaluating non-mortality outcomes in survivors. The recent Life After Pediatric Sepsis Evaluation study was a multicentre longitudinal cohort study of functional and health-related quality of life outcomes of survivors of septic shock. Early Career Investigator Elizabeth Killien from Seattle Children's Hospital performed a secondary analysis of the LAPSE study database to evaluate the ability of two commonly used illness severity scores to predict morbidity outcomes.

## **Elizabeth Killien**

My name is Elizabeth Killien and I am currently an Assistant Professor of pediatrics in pediatric critical care medicine at the University of Washington and Seattle Children's Hospital. I am originally from the Seattle area and went to the east coast of the US for undergraduate and medical school and came back to Seattle for my pediatrics residency training and fellowship in pediatric critical care medicine and have stayed on at the University of Washington and Seattle Children's Hospital. I applied for and began a NIH T32 fellowship training program in research methodology and was focused on pediatric injury research. I then moved into a full time position as an Assistant Professor with the department of pediatrics and division of pediatric critical care medicine at the University of Washington and had some protected time to continue research while submitting a K23 award that is focused on outcomes after pediatric trauma and other critical illnesses, in particular the factors that impact what those outcomes are. That is really one of my primary areas of interest. I have done some other work to try to expand my experience in these types of questions and so the particular area of interest related to this manuscript was in predictors of outcomes after pediatric sepsis.

## **Geoff Marsh**

So that brings us on to the use of illness severity scores. Can you just give us a sense of when they're used in pediatric trauma and injury of this kind and why they're useful?

## **Elizabeth Killien**

There's a number of validated pediatric illness severity scores that are used in various ways in research. I would say that they are used much less commonly in the clinical space. So we have the PRISM score, the PELOD score, the PIM score, these are all different scores that are used in pediatric critical illness. So the Pediatric Risk of Mortality score which is the PRISM score was developed to identify and predict a patient's risk of mortality. That PELOD score is the Pediatric Logistic Organ Dysfunction score and that was originally developed to describe and then to predict a patient's severity of organ failure and then subsequently was validated to also predict

mortality.

**Geoff Marsh**

In terms of using these sorts of scores clinically, the idea that they might be able to discriminate morbidity rather than mortality is an intriguing one.

**Elizabeth Killien**

That is correct and in particular one of the drivers across pediatric critical care and looking at predictors of morbidity is that the number of children who are experiencing mortality in pediatric ICUs has been declining very steadily over the past several decades. And so current PICU mortality is just under 2% of all ICU admissions for children. With that declining mortality comes two different somewhat related questions. One is that mortality is no longer a very efficient endpoint to use in clinical trials or in other clinical studies because it's an endpoint that doesn't occur very frequently and so you need very large sample sizes. The other point that comes up when mortality is so low is that it has been quite well established over the past several decades, increasingly so just in the last five to 10 years, that there's a range of morbidities that patients experience after surviving pediatric critical illness. And this ranges from functional impairments, impaired health-related quality of life, family impacts, social impacts, educational and school impacts. Social, emotional and financial morbidities that patients and their families experience after a child survives a pediatric critical illness. And what is very challenging is to identify the patients most at risk for these types of morbidities so that we can start to target interventions to improve their long term outcomes.

**Geoff Marsh**

That sounds like quite a tricky population to follow up but that has been attempted in the so-called LAPSE cohort study- Life After Pediatric Sepsis Evaluation. Can you tell me about that and your involvement in it?

**Elizabeth Killien**

Yeah. So LAPSE was a large prospective cohort study to observe and identify the changes in functional status and quality of life as well as family impacts among children surviving severe septic shock. And so these were the sickest of the sepsis patients that were admitted to these pediatric ICUs. And so what the lab study did was to identify that a very large percentage of patients surviving severe septic shock had impairment and decline really, from their baseline to their follow up functional status and quality of life. The second objective of this study was to really try to determine whether quality of life decline was prevalent enough and meaningful enough, clinically meaningful enough, to actually be incorporated as an endpoint in an interventional clinical trial in addition to mortality.

**Geoff Marsh**

So essentially, as you said, you did this secondary analysis, and very specifically you were looking at those commonly used illness severity measures and their ability to predict morbidity outcomes in these children who'd experienced septic shock. Tell me what the outcomes

specifically were and what your hypothesis was when you ran the analysis?

**Elizabeth Killien**

Yeah, so the outcomes that we looked at were the 28 day or hospital discharge functional status, whichever came first, and that is based on the Functional Status Scale which is a measure that looks at a patient's function in a variety of domains. We also looked at quality of life, that was assessed at 1, 3, 6 and 12 months after discharge.

**Geoff Marsh**

And to clarify, the illness severity scores that you were looking at were the PELOD and the PRISM scores that you mentioned earlier.

**Elizabeth Killien**

Correct. And so those were our two primary exposures and so we looked at the PRISM and the PELOD scores. And so our goal was to see whether they could predict those outcomes and so looking at prediction is a little different than looking at association. We looked at the PRISM and PELOD in a few different ways. PRISM is collected at the time of admission and reflects the most abnormal values from the first 12 hours following the PICU admission. The PELOD score estimates organ dysfunction in the first 24 hours and then again daily so you can recalculate a PELOD score every day. And so we looked at the first PELOD score, the admission one, the highest PELOD score and then the cumulative score.

**Geoff Marsh**

Tell us then, what was the predictive ability of those different illness severity measures in those different formulations?

**Elizabeth Killien**

We found that prediction of functional morbidity at 28 days had the highest area under the receiver operating characteristics curve based on cumulative 28 day PELOD.

**Geoff Marsh**

That sort of makes sense given that you said the cumulative PELOD score captures the illness severity over their entire stay in a PICU?

**Elizabeth Killien**

Correct. And that was the reason that we wanted to look at it, to determine how good are these admission severity measures which are often the ones that are most commonly used. How good are they really at establishing the outcomes compared to measures that are more reflective of longer term illness severity.

**Geoff Marsh**

And did PRISM work as well?

**Elizabeth Killien**

The admission PRISM score had an AUROC of 0.63 for new functional morbidity at discharge which is slightly better than 50:50 but not much. However, all ways looking at morbidity were better for predicting functional morbidity at discharge compared with predicting quality of life deterioration and so the best prediction of quality of life deterioration at three months was, again with the cumulative PELOD but the AUROC was only 0.71.

**Geoff Marsh**

And is that just because health-related quality of life is just so multifactorial or is it the amount of time that's elapsed between your measure and your outcome?

**Elizabeth Killien**

So we had our primary outcomes of the functional status at discharge and then the three month quality of life decline and one of our goals was also to see how that changed over time. And so we looked at quality of life deterioration, also at one month, six months and 12 months. And the predictive ability was worse, the further from discharge you got. And that's not surprising but it does really highlight that quality of life is a very multifactorial measure. And it includes the perspective of the family member who's answering these questions on behalf of the patient. And the perspective can change certainly, but also the contributors to quality of life are influenced by factors beyond the PICU stay.

**Geoff Marsh**

I liked your conclusion in the paper because whilst on the one hand, it's disappointing that you don't have this really good predictive tool for measuring health-related quality of life outcomes, it means there's some scope for intervention to improve long term recovery after a septic shock because there are obviously some presumably modifiable factors that you could target.

**Elizabeth Killien**

Exactly. If quality of life outcomes three months, six months, a year after your ICU admission were determined largely by how sick you were when he showed up, the writing's already on the wall in a way. But if it's not very predictive of that then that inherently means that there must be other things that are contributing to your quality of life and we still need to do better work to figure out what those factors are but it at least opens up the possibility that those could either be post-admission ICU clinical factors and that's a nice area that we have potential to intervene on in terms of the types of medications we use, the type of ventilator strategy, sedation strategy, how we're able to help patients start to recover faster even while in the ICU with early physical therapy and mobilization, earlier extubation, earlier weaning of sedation, there's a lot of efforts going on in that realm. But then also all of the potential factors that could happen after an ICU discharge certainly are impacting patients' quality of life and we just need to do better at figuring out what those things are so that we can figure out both the factors that impair quality of life after discharge, but also the factors that are helping kids recover and maybe we can capitalize more on what's working for some families in terms of their resilience from the severe illnesses.

