Viscoelastic Assays to Guide Therapy in Children with Acquired Coagulopathy - Pediatric Grand Rounds Meeting Recording – 1-30-2026

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58m 40s

Kamat, Deepak M started transcription

Calderon, Delia 0:03

Did you hit the view already?

Kamat, Deepak M 0:06

Yes, I did.

Yeah, this is speaker.

We'll see. We'll.

Good morning and welcome to Pediatric Grand Rounds. The CME code is in the chat box and we'll keep repeating it every 10 to 15 minutes. It's my great pleasure to introduce this morning's Grand Round speaker, whom I know.

For many, many years, Doctor Arun Saini is Associate Professor in the Division of Critical Care Medicine in the Department of Pediatrics at Baylor College of Medicine and Texas Children's Hospital in Houston. He's also core faculty in the Center for Translational Research.

On inflammatory diseases at Baylor College of Medicine, he received his MD and then completed his pediatric residency in Delhi, India. And after moving to the US, he completed his residency in pediatrics at Children's Hospital of Michigan. And that's where I worked with him for three years during his residency.

Training. Subsequently, he did his fellowship training in pediatric critical care medicine at Washington University in Saint Louis. He also received his miss in epidemiology in clinical investigation track at the University of Tennessee Health Science Center in Memphis.

His clinical and research efforts focus on improving treatment strategies for coagulopathy in critical illness, particularly sepsis induced coagulopathy. Dr. Saini, thank you very much for accepting our invitation.

We are looking forward to your presentation. The floor is yours. Thank you.

Saini, Arun 1:53

Thank you Doctor Kamat for your kind introduction and for the invitation and good morning everyone. I hope all of you are staying warm in this Texas winter weather. So as Doctor Kamat mentioned that I'm a pediatric intensivist.

Some of you must be thinking like why a pediatric intensivist is talking about coagulation. And then the short answer is that that as a pediatric intensivist, we see most patients who develop acquired coagulopathy in the ICU setting and often we don't have.

Gary Francis 2:23

OK.

Saini, Arun 2:28

Expertise of our hemato-oncology Dr. to manage this patient who often require therapies within minutes to hours and that's how my interest in this area developed during my fellowship year and then I've been working on it.

I know as Doctor Thomas said in the audience, there are a lot of general pediatricians. There are people who work only on outpatient setting and some of you are the resident or working in acute care setting and a few of you are maybe working ICU.

So I'm just wanted to go over this presentation where I'm going to introduce few new concept and hope those concepts are helpful for you to use in your clinical practice or just increase your knowledge base.

And for for future. So as you can see that the title of my talk is viscoelastic assays to guide therapy in children with acquired coagulopathy. So it's a kind of mouthful. So I kind of break it down in a subsequent slide what I mean by that.

That's it.

Just before I start my presentation, I have no relevant financial and non financial disclosure for this presentation. And during this entire presentation, my focus is threefold. First, just to give you guys a clinical context of why understanding. Acquired coagulation disorder is important for us as a physician, especially those who work in acute care settings and what has changed in our understanding of coagulation in past couple of decades and how a newer coagulation assay assessment, especially looking at qualitative function of the coagulation.

Coagulation can improve how we can assess patient with coagulation disorders and provide therapies. And then I just want to go certain cases with you guys to kind of give you a practice run how to use this asset if you have access to them in.
Your clinical practice and then I'll end this presentation with some take home messages.
So acquired coagulation disorders, it's different than congenital coagulation disorder. Congenital coagulation disorder have some specific deficiency of certain factors and our hematologist colleagues are very well in managing those patients.
What acquired coagulation disorders are the disorders which patients develop abnormality in their coagulation in the setting of critical illnesses that historically when we used to think of this disorder, we often thought about a bleeding patient who has a decreased ability to make.
Clot or hypocoagulable state. But as our understanding has evolved over the time we had understood that patient during their critical illness can be in a hypocoagulable state means like they have an increased tendency of bleeding or they can go into a hypercoagulable state which is the tendency to make clots, especially we've seen a lot of our.
Kids are developing D5th thrombosis or have micro thrombosis, small thrombosis and the organs and causing organ failure. But in our day-to-day practice and at bedside practice, we have noticed that these patients often are going to this status can be not static.
Dynamics. So a patient in their isostate can start with hypercoagulable state, may go into hypercoagulo or mixed state. Maybe they are clotting in some area in their body and actually bleeding in somewhere in the body and that makes this disorder very complex and often very hard to assess at bedside when looking at patients.
Patient who's not only bleeding, but also clotting their microvasculature. So that's the first kind of a chain in our understanding that acquired coagulation disorder encompasses not just the hypercoagulable state, but they also include hypercoagulable state. And often these states are dynamic and patient may be in mixed state, a combination of both high.
Well, I.
And in the what kind of patient we see acquired quadropathy. So the percentage is depend on the underlying disorder at this table over here showing percentage of patient who can develop acquired quadropathy. So any major trauma like motor vehicle trauma.

I need severe brain injury or or especially sepsis. A major surgeries like a surgery for heart brain tumor, major spinal surgeries, our oncology patient, a patient with post oncology microangiopathy or infection.
Like a other microengine like a hemorrhagogenic syndrome, TTP rheumatological disorder cause vasculitis. Many of our patients in ICU now require we call it extracorporeal support either heart lung machine or ECMO. They sometimes require ventricular assist side to support their heart failure or many of our patients go.
And now renal replacement therapy or CRT and of course the medication like hepalin and warfarin which are anticoagulant can all lead to a acquired coyalopathy in our patients in ICU setting and in acute case setting.
And I'm sure some of our patient now was outpatient and they also taking anticoagulation and those patient population is increasing in past decade or so.
So why it's important, why we we care about patient who develop acquired coagulopathy is because as we have started to notice that if a patient in acute care setting or iso setting develop acquired coagulopathy, they have likelihood of more severe disease and this more.
Disease associated with the worst outcomes. So if a patient and I still have thrombocytopenia, the likelihood of mortality compared to those who do not develop thrombocytopenia is about 18 times more odds. Similarly, if you have a DIC in the sepsis patient, inpatient mortality is 3 to four times higher than those who do not.
Or develop DIC and a patient with trauma abuse coagulopathy, especially if they develop coagulopathy while they are already in the emergency department. If they present with coagulopathy, their mortality is much higher than those who don't. So in essence, if you have a patient with coagulopathy, they are likely to be more sicker and more likely.
They would have increased morbidity and mortality and then that's where the emphasis is how can we improve this patient outcome by decreasing morbidity and of course decreasing mortality and then.
To do that, we have to mitigate acquired coagulopathy and how we can do it. This what how I think we can do it is to order to understand acquired coagulopathy, we need to actually have a slightly.
Better understanding of underlying coagulation system, what actually our understanding of coagulation system and how we can use those basic concept in our understanding of acquired coagulopathy. Secondly, over the past decade or so, we

as a better clinician.
The limitation of plasma based coagulation assays and coagulation assay which just provide you specific numbers to a more functional evaluation of clotting system where we understand the overall clot formation dynamics and how these clots function in terms of.
Function in terms of strength and stability and that actually has started to provide us much better information. And of course using those tools and information we a knowledge base of coagulation system, we can actually apply more target intervention whether it can be.
Blood transmission practice or it can be certain medications like anti-fibrillary agent or anticoagulant and eventually that would all lead to improved clinical outcomes. So this brings to the my first part like what is?
New in our understanding of coagulation of fibrinitic process and I'll start with that as we all remember medical schools trying to learn coagulation cascade and I never able to learn all this stuff I memorized multiple times.
And I always fail to always completely remember the exact steps goes in extensive system or interest system. But what it was that in 1949 to 60, a very elegant model of coagulation was proposed by Doctor Mark McFarlane and and Doctor Ratnoff and they said.
It's a biochemical process where activation of either intrinsic pathway or extrinsic pathway leads to a cascade of biochemical reactions which are amplified at each steps and eventually activated factor 10A, factor 5 calcium phospholated, which is sort of.
Common pathway increase breakdown of protein to thrombin and thrombin is what basically breakdown fibrogen to fibrin. Fibrin is the protein which makes the the jello or.
Frame meshwork for the cloud and then factor 12 sort of a stabilize this by cross linking and that was the understanding of our moral that there's some coagulation proteins and they're kind of activated by certain.
Insert like other extrinsic system which is tissue vector mediated or intrinsic system and that that cascade leads to this clot formation and what we have is we measure this adequacy of this system by either PTINR which we often associate with extrinsic system.
Assessment or we use partial thermal time to look at intrinsic system. We can measure the fibrogen level to kind of make sure that there's an adequate fibrogen

level and of course we can measure individual proteins in certain settings, but this is what we used to do to assess the system.
What is interesting is that in this system, Doctor Mark Fahlane and Dr. Retoff did not consider cell as a bigger component. They assumed that the cellular component is just providing a phospholipate surface to these reactions to occur.
And and that's kind of with our understanding of coagulation kind of in a bigger picture in early 1960s to 70s. But what changed in last three decades or more so in early 2000 is that we.
Understood that this process is not as separated in our blood as we learned in our medical school. So we don't have intrinsic X-ray system kind of as separated as in our blood as we thought of and actually it's a very system where.
Cell cells play an important role. Those cells are tissue factor bearing cells and the platelet. They actually are very intrigal to a current more accepted model which we call a cell based or physiological model of coagulation.
And what happened in this system is that whenever there's an injury to vascular endothelium, the tissue factor banks and like such as micro fibroblasts get exposed. These cells generate small amount of thrombin.
Which by activation of factor 10 and this small of amount of thrombin activate the platelet in the vicinity and this activated platelet further generate more thrombin and more factor activated factor 10 and basically.
Start recruiting more plates and as the amount of thrombin generation increase to thrombin burst, that thrombin burst leads to the cloud formation. So the process where we learn is intrinsic pathway, extensive pathway to change to.
Initiation, propagation and amplification and a process where only biochemical reaction was more important to the process. Now we understand the cells are very integral in regulation of amount of plotting and the site of plotting. So that's kind of the change in our.
Understanding of how the coagulation is different, how the coagulation process occur in our body. But in reality actually it's way more complex and I I can spend days just talking about the complexity of coagulation system, but what I want.
You to take from this particular slide is that in order to make the clot in our body, we need plasma factors, we need cells and and the flow within the the blood vessels determine the quality of the clot and this clot actually are distinct.
Based on what factors are driving it and the properties can be how they form means the formation and breakdown kinetics work with the composition of these clouds

which can be different different diseases and that changes their structure and that structure determine the functionality of this cloud.
And how permeable this clot going to be, how stable this clot is? And then that's kind of a very new understanding and the the more recent literature suggests the plot composition, plot structure and plot function can have implication not in just acute care setting, but actually in chronic illnesses like.
Risk of infection, risk of risk of stroke, risk of peripheral vascular disease in patients with diabetes and all those factors. So adults actually started to understand that clot characteristics of a patient may have implication, not only the acute.
But also in chronic lenses. But that topic is out of scope for this presentation. But if I can give you one message from this slide is that we now know that all clots are not the same and the clot itself.
Has inherit properties which is determined by the plasma factor, the cells which get incorporated and then the most important factor is the clot structure and these structures can determine the functionality of the clot which has implication on the the the organ function in our.
Critical case setting and I'll show you some example what I'm talking about the clot structure. So this is just to guys to give you an example of what we see. So this is in our labs we have a the swine model of sepsis acquired lopathy.
And what we do, we have this piglets, we inoculate this piglet with either E coli MRSA which we collected from our patient in ICU and then we observe this piglet for up to 72 hours and.
Take cereal blood samples and and as we collect this blood we study this clots made of the plasma through electron microscopy. So I show this picture. So as you can see in a piglet before any sepsis, this is how the clot looks like under the electron microscopy.
You can see the fibrin fibers are very smooth. They're like noodles like and that looks very uniform the thickness. And if you just look at it, you see like OK, this looks like a mesh of a fibrin and network, but there is a very.
Smooth pattern to it, but you can see the dramatic change happens when they has developed the piglet was inocular with Mrs. and sepsis. So you can see within 72 hours the same piglet.
Ex-vivo clots change dramatically in structure and you can see this fibers are not irregular on surface and we think this irregularity comes because the position of various inflammatory and other coagulation proteins bind to this clots which change

the property of this clot.
And this mesh becomes very dense and abnormal and the same pattern we saw actually at the piglet who was inocular with E coli. So that's saying that if you make a clot for a patient who's not infected was infected, there is a distinct change in the structure.
And the the function of this clot and when we study this function, a clot function like permeability and the strength, we found these clots are less permeable when the the piglets have sepsis and they also are harder to break down.
But does it occur in the patients? So uh, this is uh uh uh reminds them uh the the the study we did during the COVID uh pandemic. So I know we all uh went through it uh early uh uh 2020-2020 and 2021.
And if you can all recall that most of our poor patient has extensive thromboembolic complications, more so in adult than pediatric. But all this patient had and their autopsy finding a microvascular thrombosis in their lung vasculature. They had higher.
Incidents of deep vein thrombosis, a lot of silent MI and stroke in adult population.
And so this study which we did it in our adult ICU in the Veteran Affair ICU at Houston VA Hospital, what we found is.
The abnormally in clot structure. So I'll just walk you through this slide just to kind of Orient you. So what we did is this is the plasma of a patient we collected either those who are healthy or those who are admitted in ICU with sepsis associated with non COVID etiology and then sepsis because of COVID.
And in order to see the the the fibrin structure, we added fluorescent fibrin in their plasma and use confocal microscopy to like a look at this clot under the very specialized confocal microscope and you can just see looking at the clot structure in healthy patient we have a very well.
Fine kind of a clot structure. There's a lot of black area means these clots are forming, but they're not very dense. But when you're sick, this clot structure becomes denser and there's the fiber becomes less thicker and there's less room, but.
As you can see that COVID patient has dramatically increased density of clot compared to non COVID sepsis and this patient when we compared for sepsis with non COVID with COVID, they actually had similar severity of illness. So it's not that severity of illness was driving their.
Structure. And so that's where it is like so though patient has a COVID infection, we realized that this patient has abnormal clots and that was the reason why this patient

actually having more severe organ dysfunction and more thromboembolic complication. And I don't know if you guys can all recall that very early in the course of.
COVID patient, we started using anticoagulation of any patient who was admitted in an ISO setting, both in adults and in a pediatric setting, which is very unusual for us to use anticoagulation in a patient with viral infection. But that was how we understood and how this knowledge.
I will not go to into details, but now actually we understand why these plots were denser and what's driving it is it's because the the COVID patient have this viral spike protein which get shed during the viremia and this spike protein can directly bind to. The protein called the fibrogen as the protein and when it's bind to this fibrogen protein, it changes the clot architecture and actually been discovered and published in a very, very elegant work in nature last year. So that's where we kind of understand what mechanism.
Is actually driving it. So this is just the context of our coagulate our industrial coagulate system is evolving from a very simple biochemical model to a very elegant model to a cell based model where the process is different to now even.
That plot of structure and function is maybe the new way to assess that quiet. So this brings to my second component of my talk is how it what?
Can we do to better assess our patient acquired coagulopathy and we start to realize that just mere measuring the number or quantity of coagulation factor or quantity of platelets or quantity of fibrogen may not be sufficient for us to understand the underlying abnormal.
Quality in cloud function and and and and and and then to in order to understand that better we need to have certain qualitative ***** which can improve our assessment of how these clots are falling and what.
Kind of a function or strength they have so that we can kind of translate that into a therapy. So that's kind of a where the viscoelastic assays come into the play and I'll tell you why I I think and that new and upcoming literature suggests that yes viscoelastic assays can help us better assess patient with.
Acquire coagulate again. So going back to comparing plasma based coagulation assay and viscous. So as we all know that we will be very well worth in interpreting our.
Plasma-based coagulation I see that we are doing it to many years and they're very useful. I'm not saying that we don't have to use them as if they are actually very

useful that both thrombin time or INR, partial thrombin time, fibrigen, platelet, D dimer. So extrinsic pathway, partial intrinsic pathway, fibrigen, just a protein if it is low can have.
Abnormal PT and PDD plated counts is very obvious and D dimer is kind of marker of how much clot is lysing. But what all of this plasma assay has the limitations. First, they don't tell us the quality of the clot forming. They don't. They don't tell us how. What is the strength of those clots are? And also they don't tell us if the patient has a hypercoagulability. It means like are the patient are at high risk of thrombosis and clotting in microvasculature, something which we really need to know in our IC patient.
In comparison to that, viscoelastic acids are where we measure the clot formation in whole blood sample and what it does, it actually provides a more global understanding of dynamics of clot formation over time and actually provide us some some assessment of clot strength.
And the beauty of these assays are that that not only give us if the patient is at risk of bleeding, but it also give us some indication if the patient is at risk of clotting. And that's actually very helpful for us to kind of guide therapies or minimize excessive transfusion or initiate anticoagulation in the patient who are in the the.
C or acute case setting. And so that's kind of why I feel viscoelastic cases have they use an importance and then those who have not used this viscoelastic have not heard of this, I'll kind of walk you through what they are and how they work.
It's not new actually the the 1st and early invention of viscoelastic acid happened in 1940s and and then over time the technique has more refined and become available to bedside physician. Now we can do viscoelastic acid within the emergency.
Department we can do in the ICU or we can do the OR. We can actually have platform where we can have this viscoelastic assays read live when the cloud from the when the machine is reading we can actually see the live generation of certain assays numbers and we can actually.
We don't have to wait for hours for lab to do PTT and other factors to measure it and get back to us. We actually can see in real time within 10 minutes to 20 minutes and can do intervention. So it really can save a lot of time and can have a faster we can have a faster response to.
Our patient needs. So I'm going to talk about that we can actually do viscoelastic assay and initiate clot formation in whole blood either by kaolin which mimic the intrinsic pathway activation or we can use tissue factor which mimics the extrinsic

pathway activation.
And because this is whole blood and accounting for both the platelets other the white blood cells, so it basically provides more, it's more closer of a mimic or in vivo condition in the patient and more physiological.
And it as I mentioned in previous slide, it provide us the dynamics of clot formation and oral clot stand but give some information about the adequacy of platelet function and how these clots are lysing or fibrillistic pathway and that that information is unique to this assay which has not been provided.
Added by our class and this essays.
So this brings us to what are they? How really we do? What is the technology behind it? So this is a complex figure, but I can walk you through and actually give you a very easy example to understand what's happening.
So if you can consider a clot as a jello and as many of us have made jello at home. So when we make jello we boil water, we put the jello powder and let it cool down. As it cool down the the the the the water which is liquid turn into jello like.
Consistency and the longer we let it settle and put the colder water, the thicker it become. And then if you put a stick in it, the first you put a stick you can take it out. But when the stick stays in and then the jello kind of form completely, you cannot take the stick out, it gets stuck in it. So that's essentially is the basis of viscoelastic SA if you get anything out.
Of my presentation. This is it. We make a jello of the whole blood in in a cuvette and we suspend a stick, which is we call it a fixed pin. In tomboelastrography, we move the cuvette, we move the cup oscillate 180 degree both sides and we see if that.
The the pin which is suspended started to move and once the jellos get thick enough of the whole blood, the pin will start to move and as it starts to move, it creates the torsion tension in the the wire and that device has been censored and basically relating to a graphic presentation.
A different form of a different platform of viscosity. Let's call it tombolastrometry, a rotation tombolastrometry in this. Actually the only difference if looking at is that instead of moving the cup, we move the the the the suspended pin and the pin actually moves a lot early on.
But as the the jello gets thicker, this pin started to move less and less and that change in the the movement of the pin is sensed by optical sensor and that again give us the tracing of thromboelastographic tracing or low temp tracing. And there's a new evolving technique which many of you I don't know if have your system is

called thromboelast.
Six S platform which consider a more cassette based setup. The reason using this technology is that many of these assets require larger amount of blood. So to minimize the amount of blood we use, especially in our neonatal population, the company came up with this new technique called.
Thumbelastography. What happened in this technique is that instead of having the cup, we have these channels and we basically put the blood, blood goes through and get in those small cup like channels.
And then they said the bottom of this channels are open and then the clots start to form and then it missily make a gel like consistency and then you wiggle this gel and see how much wiggle is there and those wiggle in the that the clot jello.
The vigil in the clot kind of measured by this optical sensor and actually give us into the number. So that's kind of a different technique, but I hope this kind of give you a context. So we basically make a gel of the blood. We suspend the stick and see if the stick is moving the the movement of stick is either sensed by the Togen.
Or by the optical sensor and give us a number and the tracing. So that brings us to what tracing we get. So this is the tracing we get, which is a very classic tracing of thermoelastography. So the X axis is time in minutes, so often the thermoelastography can be read from.
From zero to 60 minutes and and some situation you can go up to 90 minutes. So time is usually in minutes and can run the the one test can run up to an hour, sometimes 1 1/2 hours and then the Y axis is the thickness or a millimeter which is basically how far the graph is separate out and then it comes in so.
And then there are certain parameters we have for this. That parameter we call it the R time or reaction time. We call it K time or or K kinetics. We call alpha angles, maximum amplitude lies at 30 minutes. So those are the the, the.
5 parameters we can read out. There are more parameters, but you know for sake of this presentation I'll stay on this 5 parameters and then the R time is is the surrogate of prothromed time or partial thrombin plus time based on what kind of activity you use to generate that. So remember when we.
Do plasma based assays. The only information we get is the R time. We don't get any information beyond that. We don't know the dynamics of fibrin polymerization which is scale time. We don't know the the strength of the clot and we don't know how this clot is licensed. So this.
4 parameters are actually additional information we get from viscoelastic assay,

which we do not have do not have from our Plaza based coagulation assay.
The rotem, some centers may have rotem and rotem is basically very similar in terms of tracing. It basically again accesses time in minutes up to 60 minutes and then amplitude in millimeter and then our time is basically labeled as plotting time in the rotem reading.
K time is called being labeled as cloud formation time Alpha angle means Alpha angle and then maximum amplitude is kind of been labeled as a maximum cloud form this and of course license index at 30 minutes and then you can have maximum license at like end of the tracing in 60 minutes.
One distinction between tag and row time is that in tag we is 1 tracing other can be reflective of extensive or interesting. But in row time we actually get four different tracing in in through one sample so.
It can have X time where we activate the clot from tissue factor. It also give the tracing of intrinsic pathway and then it one tracing called fifth time where basically we the the the clot is only accounting for the the.
The effect of fibrogen in that clot, it basically indicate the effect of platelet by putting platelet inhibitor and then we also have we call aptam or aprotatin time which basically blocks any kind of fibrillosis. So tell us if the fibrillosis is is hyperactivating these patients so.
Within within a single tracing row time we can know the tissue factor mediated clotting. We know intrinsic paths mediated clotting. We can know what's the contribution of the fibrogen and we can also know if the fibrillus is is playing a role in our clot.
From a breakdown and all this information can be used in intervention so. Understanding what's the, what's the technique? Understanding the the different parameters we get from like a like a standard at a tracing from Rotem and and then thrombography. How can we use them technically? That's the question often my colleagues ask me Arun.
What can we do to use that? So there is some guidance and I'll walk this through because that's something we do use clinically. So there are 5 parameters which we can often pay attention to. As I alluded in previous slides, the reaction time are plotting time. Basically it reflects the the early plot for.
Information we have defined normal range. This is more well defined in adult population than Pediary, but we have now normal ground for Pediary population and if it is prolonged, it suggests there's a deficiency of a component in the plasma which

is usually the clotting factors in order to.
Fix that we often transfuse plasma which is contained various clotting factors. If we see changes to the clotting K kinetic or clot formation time and it is prolonged, it suggests that fibrin polymerization of is limited or.
Lacking either because there's a dysfibrogenemia means the fibrogen you have in the blood is not working well or there's a lack of fibrogen and to or to or to collect hypofibrogenemia or dysfibrogenemia, we use cryoprecipitate which has higher concentration of fibrogen and few additional clotting factor.
And OK, alpha angle is similar, reflecting the same thing but a different parameter. Once we go in from there to the maximum amplitude, we look into whether the maximum to less and more. If it is less, it is fine either the platelets are lacking or the fibrogen is lacking and we can transverse plate and if there's excessive.
We can actually correct it by using anti-fibrillary agent or TXA. So these are the numbers we can use. Some people actually believe in just looking at the the tracing globally and kind of compare with the normal tracing. So that's another way to kind of look at just looking the tracing over time you can use to it. So this is a normal looking tracing.
If the R time is prolonged, it looks like this. If the platelets are low, you set a low MA. If low fibrigen you can have a very kind of pointed long tracing like and if the both platelets and plot effects are low, you can have a low MA and prolong R time.
If you're pro thrombotic, which is extra, you can see increase in the MA only because increased because of platelet hyperactivity. If it is a short hour time, it is because of the excessive clotting factor activation and our combination of both. And then if you have a clot lysis, you can have a significant.
Memory fibrillosis as you can see in this taping out very significant lysis versus you can have rapid clot formation and then secondary lysis often seen in DIC. So there's a very various way to integrate this tracing either go by numbers or go by the tracing itself, but definitely help us.
Distinguish bleeding tendencies versus thrombotic tendency versus hyperphalmotic stage and those are extremely helpful for us as a better physician to use and apply.
So this covering those two aspects, I just often feel people still struggle to use this at best. So I thought, how can I explain them better? So the only way can I explain them better to you guys is using some clinical scenarios. So these are.
Truly a real patients we manage in ICU, I can change some numbers to just make it a little bit easier. But these are the true clinical scenarios we often face in our ICU. So

but the first example is a patient who's usually 10 year old who has a leukemia. Has underwent transplant and now presented from EC in sepsis. He's in shock. Come to our ICU. We draw some labs. We found a patient is thrombocytopenic with platelet count of 25,000, has slightly prolonged IR with two and plate and slightly prothombin.

Thermopathic time 40 seconds patient not actively bleeding, but because patient has been sick and required a high dose vasopressor, we as a bedside physician has to put a central line. Then the question is should we trust with this patient or should we just go ahead and put a central line and that's where the beauty of our.

Scholasticus he comes in because what happened if I would transfer this patient that I need to order the blood, I have to wait for a few more hours to blood to come before a transduce patient may not get adequate dose of a suppressor which will prolong his shock stage, may worsen his clinical state and may cause organ injury to expedite that process.

I did thermal ostrography. I got this tracing and I look at this number. As you see the R time falls within the normal range, so is the K, so is alpha and the maximum amplitude and lysis. Just looking at this tracing, even if you go back the previous slide that the tracing looks pretty normal.

So just looking at this, I can say that patient actually has a very, though despite of thrombocytopenia and some lack of coagulation factor, overall clot formation potential and clot stability is is preserved. So and and patient is not actively bleeding and I'm doing a low risk procedure, so I don't have to wait for anything.

I just can go ahead and put a central line. So not only I'm saving 2 transfusion but also saving time and maybe faster recovery of this patient from septic shock because adequate vasopressor early on correcting stop state shock state may improve my patient outcome.

So another example of using tech is a patient who often present in us is with a motor vehicle accident and now has a moderate trauma. He has a traumatic brain injury based on injury, CVT score and patient is still having mild ongoing wounds and bleeding.

We did the the the labs and we say INR is about two platelet count is the partial somat time is 4038 second and platelet 120. So sort of some coagulopathy but not severe. A vertebation is bleeding so and and you want to know do I need to trust this?

Patient something more or anything else I can do and we call it this rapid tag which

give result within 30 minutes where basically you're only getting the information of fibrin point measurement. But this rapid tag numbers are here. What you see in this table is that patient has normal R value because normal K.
Value normal alpha and actually slightly decreased MA means like patient is making clot but not very strong, which makes sense that patient has some degree of thrombocytopenia which might be playing a role. But what is most profound in this tracing is the severity of clot lysis. So patient is lysing this clot very rapidly.
So this is a very common state called primary fibrillitic state in early stage trauma in this patient. So which is is extremely common because the treatment of this is actually not giving more transfusion because that's going to just make this patient hyperfibrillative state worse. The treatment is anti-fibrillic aged or TXA.
So giving TXA of this patient in within the emergency setting may the patient outcome by decreasing the excessive bleeding which decrease the exposure to the the blood transmission and may be able to get the patient to or safer and faster. And that's very well described in the literature and I'm not just telling that that's.
We have determined that early trauma in this coagulopathy actually is hypervermatic state and if it is present increase the mortality by 10 to 15 times if it is not present and actually apart from the surgical building controlled TXA within six hour of trauma has been been.
Been used as one of the agent to minimize the bleeding. Of course do what called balance transfusion practices in our trauma patient MTP with one to one to one ratio and of course limit crystalline and permissive hypertension. So the role of TXA over here is much clearer because not.
All patient would benefit from TXA, but without by doing the thromboelastography we can define those patient.
Another example is a very classic patient we see often is the patient who present with acute liver failure in the setting of viral hepatitis. This patient has a INR of 3.5, PDT of 30 seconds, some thrombocytopenia, fibrogen histogram.
No active bleeding and you know often this patient with INR 3.5 we get worried that patient might have a life threatening bleed and should we prophylactically transfer this patient. But that has inherent issues because the only marker, one of the marker we use to have a patient to list for transplant in our liver failure patient is IN.
So if we artificially correct the INR by giving FFP, we would lose our ability to monitor the severity of liver failure or timing of liver transplant if the patient requires one. So in this kind of scenario, can we do thromboelastography and kind of better define

the underlying clotting?
Cloth formation and cloud function. So as you can see again just going back to the tracing, it looks a very normal looking tracing just looking at from the graph tracing number. But then you go specific numbers, all the numbers are fall within the normal range. So it reassures me though despite.
The patient has liver failure, patient has elevated, but overall clot formation and function is preserved so I can sit on the patient. I don't need to do any intervention. I just have to monitor the patient and that preserve my ability to monitor patients simulated fitness and have a timely intervention if patient required transplant and. Listing for that and and this again has been been shown in the literature that the coagulopathic liver failure is different and it's called a rebalanced coagulopathy because the degree of the lack of anti hemostatic agent versus prothromatic agent is kind of is happening all different component of.
Coagulation system, whether it's primary hemostasis, coagulation and fibulsis. So that creates though there's a decreased thrombocytopenia, but there's also high von Blur factor and low MTS 30. It's going to balance out that the primary. As there's a decrease in the procoagulant factor, there's also decrease in the.
Anticoagulant factor. They also decrease in hemostatic factor like protein C protein. So all this kind of balance it out and so is fibrinosis. So in the end the liver failure patient do have abnormal coagulation but everything is in a balance. We don't have to intervene in this patient because this patient is not at risk of bleeding and our. The the case example. So another example is a 90 year old patient with appendicitis who has severe sepsis and now coming from the OR has already ongoing bleeding. He has MTP was activated in the OR. Patient received 4 units of RBC, 2 units of class 9.
We have a patient at bedside open abdomen and actually bleeding. And the question is what should we do now? And you got this tracing which actually is very helpful. It tells you that patient clotting factors are preserved because our time is normal, but patient has very prolonged care.
Value and also very shallow alpha angle miss. It suggests that patient has either dysfibrogenemia or hyperfibrogenemia. The patient also has sigma low MA which suggests maybe deficiency of not only just the fibrogen but maybe a plate.
So in this case scenario, maybe the next step was to not only give first give cryo, and if the cryo doesn't correct your K and MA, you can go ahead and click. But the first component I would give after four year RBC is a cryo. If the cryo doesn't fix the

problem, I would go plate the transfusion.
We can also do both together, but maybe the crowd may be the first appropriate step to go.
Another case example, I'll show you guys a case of a 14 month old patient with cerebral sepsis who's multi vasoactive intrusion. You know, it's a classic patient of meningococcaemia and we often see, though it's much rare to see meningococcaemia, but we often see one or two patient with meningococcaemia. In our ICU and this patient is here has thrombocytopenia, has prolonged PTA and prothombin thromboplastin time, has heaviness of kidney injury and liver injury. So this is a classic.
The sub-phenotype of sepsis, we call it thrombocytopenia associated multi-organ failure and we start to understand this is the phenotype where we have the highest mortality in our patient and what you're seeing is a tech tracing and tech tracing or here is reflective of some degree of consumption of coagulation.
Factor so the R time is slightly prolonged. The K angle is also slightly prolonged. I'll find the MA is shallow but definitely some lysis. So this is sort of a classic intermediate stage of DIC. So in early DIC we have hypercoagulable state and rapid lysis. Intermediate DIC state is where.
The consumption started to happen, but not yet widespread. But patients started showing the sign of both the some degree of hypo-quality state. So this kind of patient, what can we do? Because patient has passed the early hyperfigmatic stage, so TXA may not be the right choice what we can.
We can do is a plasma exchange where we can taking away correcting a lot of coagulation factor and we're taking a lot of factors which are driving this DIC and there's some evidence to show that early plasma exchange in a patient with intermediate DIC and Tamo phenotype may have benefit and now.
It's one of the the recommendation are still weak, but now it's one of the recommendation is a patient to consider a plasma exchange in a patient with sepsis of phenotype of thrombocytopenia with multi-organ failure. The last patient I want to kind of talk about, it's very complex, but you know, just some of our.
IC colleagues are here who use have a patient ECMO. It's sort of kind of show that not only in acquired from different condition, even in ECMO we can use this this as a tool to guide therapy.
So an example of a four year old patient who's with a RDS was on VV ECMO for day two. The patient has mild ongoing cannula side bleeding and we do a multi-facet

coagulation as you can see we do activated plotting time. We measure INR, platelet and thromicity level.
Partial thromb impassive time, anti-tannin level which reflects heparin effect and then heparin fusion running at 50. It's kind of a complex patient with so many things. The beauty of a thrombolastrography is that we can have a standard attack tracing which may look like this. This is very prolong our time.
And a very shallow alpha angle and very low MA. But we can also negate the effect of heparin by putting something called heparinase and we can have a tracing which tell us the underlying clotting potential of this patient. And happiness tag is very different than the Kaolin test. So when you look at the heparin tag, you say everything looks.
Pretty normal. So if we negate the effect of heparin in this patient that the patient ability to make clots actually pretty normal. So the what's going on in this patient. So maybe the problem is too much heparin. So though the antigen level is .9 but despite of that patient may have a significant heparin effect shown by.
The delta are basically different Kaolin and heparin start. So tell us that maybe we should lower the heparin which will decrease the patient bleeding and oozing and very easy tool to use and the treatment is decrease heparin infusion. So it guide us.
How to do the transfusion anticipation? There's some data to show that thermal osteographic can help distinct bleeding and some of the computation. I won't go into the detail of that, but there are some evolving data out there.
So this brings me to the to the end of my presentation. So I hope I was able to put on the message that first that quadropathy is is common in ICU patients, especially if they're critically ill.
It can have both hypercoagulable, hypercoagulable mixed state. When it's present, it causes more severe disease and lead to increased morbidity mortality. Over the time we understood the coagulation process is more complex than just the interesting and extrinsic pathway and then clot formation and clot formation.
Function has implication in both in acute and chronic illnesses and one of the way to evaluate clot function is using viscoelastic assays which provides qualitative assessment of the whole blood clot encompassing both the cellular component, plasma component and provide us not only the clotting process but fibrinoitic path and.
And using those tools in a specific patient, we may be able to reduce the need for blood transfusion, may provide more specific anticoagulation or anti-fibrillic therapy

and hopefully that will improve the outcome of our patient population. Thank you so much for your attention. I hope this talk was useful for some.
Some of you and maybe some new information for some of you before answer any questions.

Kamat, Deepak M 54:20
Thank you, Doctor Saini. That was a wonderful presentation and educating us on viscoelastic assays, how to use them in critically and non-critically ill patient. There's a question by Doctor Sanesan in the chat box. Has there been any effort to develop standard ranges for T EGS in Pediatric population?

Saini, Arun 54:40
Yeah, that's a very good question. Yes, we have a few studies which have look into a standard coagulation like the normogram for Pediatric population and actually there is a effort towards developing normogram on neonatal population. The challenge of these assays is the amount of the blood we require.
To do the assay. So for neonatal population, there's a couple of studies out there now using the combo elastigraphic success platform, which is a microchip platform which required almost like a 30 to 40 microliter of blood compared to about 500. 100 to 750 microliter to one ML blade for the the standard of regular thermal astrography.

Kamat, Deepak M 55:27
This question about Doctor Gong, I think you partially answer that question. How about premature babies? Are there any standards developed for premature babies, newborns?

Saini, Arun 55:37
There is not enough data for premature babies just because the limitation amount of blood required to run all these assays. So but the new platform of of thermal ostrography 6S might provide a little bit more information, but I think there's studies. Still going, going, ongoing, but one M of blood from a premature baby is a lot of blood to collect and it's very hard to do. But I think when we compare to plasma based assay, maybe doing either one of them may be better than doing both and

that's I think the data is not strong enough yet as to just rely on.
Only on the scholastic assay, at least in the neonatal population.

Kamat, Deepak M 56:21
Any other questions, comments for Dr. Assignee?
So is this a routine practice to use viscoelastic assays now in the PQ's all over the country, all over the world? What is the status?

SA

Saini, Arun 56:36
Yes, so so for many. So there are certain situation. If you have a level 1 trauma center, you you require to have a viscoelastic access in your hospital system patient. If you have a center where you provide, we call it a vento classes device, you're required to have.
Elastographs in your system. In the larger centers, it has become a routine practice. Like in a Texas Genus hospital, all of our patients who are on ECMO have a Rotem done every day, so we measure them every day.
All of our major trauma patient, we do it. All of our liver failure patient pre-transplant, post-transplant, intra-transplant, we do it and all the major surgical procedure we actually can this assets can be read and done real time. So they are actually meant to be.
That side, so many ORS actually have them in the OR and you run the assay, you get the tracing, you look at the tracing and you can intervene as early as within 30 minutes.

Kamat, Deepak M 57:44
Thank you. Any other questions, comments for Doctor Saini?
I I don't see any comments or questions. Dr. Saini, thank you very much for that really wonderful presentation. I learned a lot for myself about how to use this viscoelastic essays. Thank you all for attending this morning's grand round.
I'm going to conclude and we'll see you all next next Friday at same time. Thank you, Dr. Saini again. Appreciate it. Thank you.

SA

Saini, Arun 58:23
Thank you so much. Thank you everyone for your attention. I hope you stay warm in this and another cold wave coming to Texas.

Kamat, Deepak M 58:29

Thank you. Have a good day. Thank you.

Kamat, Deepak M stopped transcription