So --- I’m Dr. David Hui from the Department of Palliative Care at The University of Texas MD Anderson Cancer Center. And we are now going to cover Prognostication in Advanced Diseases, Part III.

So in Part I and II, we discussed some of the prognostication principles and how we can estimate survival in patients with advanced cancer as well as other diseases. And now we’re going to talk about brain death, terminal extubation as well as a very important topic of how we can communicate prognosis with our patients and their families.

First, let’s touch on brain death because this is an important topic. When patients have brain death, this is really a spectrum of what we call anoxic brain injury. It goes from patients who have a chance of good recovery all the way to the worst diagnosis which is they have brain death. And the categories include persistent --- persistent vegetative state in which they are unaware, but they may be awake at times. So awareness means that patients are responsive to stimuli. And those who have persistent coma are unaware all the time. But potentially they could actually be reversible, so we have not confirmed that they are irreversible. But to make the firm diagnosis of brain death, clinicians need to have a very careful assessment of the patient prior to establishing this irreversible diagnosis.

“And why do patients have brain death?” Well, there are many potential contributors including hypoxic injury, such as a major myocardial infarction or major subarachnoid hemorrhage in the brain and those could cause the patient to die. And patients with severe head injuries or even metabolic causes may also have brain death as well. But the important thing to keep in mind is that there are some diagnoses that may mimic brain death, but some [are] actually potentially reversible and it’s important to rule out. These include hypothermia, drug intoxication as well as neurological disorders, such as Guillain-Barre syndrome.

So the understanding of this is important because we are going to discuss then how we can make the diagnosis of this major disorder of brain death. So first we need to collect the history and make sure that there is a good reason that the patient actually, you know, would have brain death. We need to rule out intoxication, rule out metabolic causes of encephalopathy as well as hypothermia because if these are present maybe they can be treated and maybe the patient who looks like they have brain death could come around. And then we need to do a good physical examination. And essentially those who have brain death the Glasgow Coma Scale is a 3, they are not very responsive to any stimuli and their brain stem reflexes. And we have to do the whole range of the testing should all be abnormal. So finally, it is important to do the apnea testing to diagnose brain death. So apnea testing essentially starts with deciding that the patient very likely has brain death. And they are usually on a ventilator, dependent on the machine to breathe. We then do an ABG to get a baseline of their pCO$_2$ level. Then we remove the ventilator and then see what happens to the patient. During that time, we’ll see whether without the machine the patient will breathe on their own. If they do, then they don’t have brain death. But if they continue not to breathe or if we monitor them and they have significant arrhythmia or drop in their blood pressure or significant desaturation, then we might need to put them back on the ventilator right away. But otherwise we wait for up to eight minutes before repeating the ABG testing. And if the ABG shows that there is an increase in the pCO$_2$ level, meaning essentially there is hypoventilation, they are not breathing, not ventilating, and the absolute pCO$_2$ cutoff is 60 or if the relative increase from baseline is greater than 20 then the --- this will fulfill the brain death criteria.
If there’s any ambiguity in regard to whether the patient has brain death, we would then proceed to do some imaging such as a brain scan that some --- can provide sometimes further information or even other as --- other potential imaging modalities that can provide further supportive evidence. So to diagnose brain death, we need to have a good history, a very good and comprehensive physical examination, and also do the apnea testing.

And here is just a study showing that patients who have abnormal brain stem reflexes upfront tend to have a very high risk of dying or poor neurological outcome after a myocardial infarction. So again, it shows that the brain stem reflexes are very important to tell us how the patient is going to do.

So moving on to the next category would be terminal extubation. And for this group of patients they actually have not died yet, but they are all on ventilators and after a while the family, perhaps in discussion with the healthcare team, decided that they do not want their loved ones to continue on a machine. And that it would be important to take away the intubation and let them die naturally. So “how do we do that properly is the question?” And I have to say in the literature there have not been too many studies. And --- So here I have included a systematic review that only looked at eight studies focusing on the process of terminal extubation. And most of these studies essentially highlighted that we tend to give medications both before, during, and after the withdrawal process for those individuals to minimize any distress that may be associated with the extubation process. The medications typically are benzodiazepines and opioids, such as fentanyl and midazolam.

And of course, I think also very important prior to terminal extubation is a prolonged discussion and make sure they understand what are the implications including what the prognosis will be and the median survival in the systematic review for the core of patients is about 35 minutes to 7.5 hours. So it is really ranging from minutes to hours, but then occasionally there is the patient who lives out for days even after withdrawal from the machine. So it is important to explain to family that even though there is rough range, it is important to be aware sometimes the patient may go on for much longer. But eventually all of these patients die in a short term. So once it has been very well established that terminal extubation is the right thing to do, then how do we extubate is another question. Well, the patients are medicated and in some institutions they would just remove the tube and that’s it. But others do a more kind of gradient approach in terms of weaning. So they would turn off the alarms for the machines, they would cut down the FiO2 to room air, they would decrease the PEEP and then cut down the machine ventilatory setting and then eventually remove the tube. Whether you do it step-wise or just remove the tube altogether, again, there is no evidence to guide us which way is better. Partly, it would be based on institutional policy as well as in discussion with the patient’s family.

Now, with all this understanding of prognostication at different disease stage, it is important to actually discuss how we can put all the signs together into talking to patients and/or their family about survival, because this is actually one of the biggest challenges for healthcare professionals.

So I think some of the key questions that we have is 1) “What kind of prognosis information do patients want?,” 2) “When should we actually discuss this kind of information?,” and 3) “How should we discuss them?” So to answer the first question, “what do patients want?” They generally want us to tell them you know the honest answer. They generally want to know not only their survival but also what is it that they can expect in the future in regard to their function, in regard to their care needs, and for some patients the thing that they actually want to know,
but too afraid to ask is how are they going to die because that can help them understand it better. And for their family caregivers, these are also important information for the caregiver to have in order to plan ahead as well. In regard to when we should actually bring up the prognosis discussion, the literature shows that some patients prefer that we discuss it up front with them when they are diagnosed of the cancer. Others do not want us to actually talk to them maybe a little bit during the disease process. And overall, a majority of them do want to know their prognosis. But there is small proportion, maybe 10-20% of patients who say, “No I -- I don’t want to know how long I get to live. I know I have a serious illness, but that’s probably good enough for me. I will the rest perhaps up to God,” they say. So how do we know then from the clinical standpoint when should we discuss it? Well, we can ask the patients and a lot of the times by simply talking to the patients and the families, talking --- discussing, “Well, many patients want to know about their prognosis. Is this something you want to discuss today?” can be a simple question leading to that. And then patients can tell us what they prefer. And the last question then is how should we discuss prognosis? I have to say there is no one single approach to discuss it. But what we thought of as maybe an art of communication with patients has now actually evolved into a science because there are more and more studies out there discussing different techniques. And in fact, asking the patients and other healthcare professionals, what is the best way to do this. So what I will highlight here is maybe a general approach and ultimately we clinicians need to adapt the approach to the individual patient. And what works best for that patient who is sitting in front of you is really the approach that you need to take. So --- But one very common question that we have is, “Well, should I tell patient the number?” You know, let’s say I think a patient sitting in front of me has three months to live. Should I tell them that you know they have three months to live? Well, I think we can take some lessons from perhaps the patient known as Stephen Gould and this is a case report from him. And he actually is a patient who was diagnosed with mesothelioma. And you know, advanced mesothelioma unfortunately is not curable and in fact when he looked up the medical literature and he’s very well read and a well published author, you know, the median survival is only about eight months. And when he asked his doctors how long he gets to live, “Well, they mentioned to him that it was about eight months.” So everything is consistent. So if this idea of eight months in his mind, but then three years later he wrote a paper saying that the median is not the message. He said that giving patients a number is ambiguous at best and both misleading and discouraging at worst. So imagine, you know, if a patient hears the number of eight months then they may make their life plans according to that number. But the truth is the -- you know, this number is just a median meaning that half the patients are going to be living less than that time and half the patients are going to be living more than that time. And very few of them actually have an eight month survival. On top of that, patients who have this expiration date of eight months, if they actually live longer than that, a lot of them start to have concerns about what to do because they have said all their goodbyes, they have make all their plans, use up their money and now you know nine months into it and what do I do. So there may be some existential concerns. And for patients, who live a lot less than eight months, well, we may be robbing their opportunities to address some of the important things they would want to do if they actually knew they have a much shorter survival. So by giving a specific number, I think, for clinicians we may be setting ourselves up for failure and also potentially misleading the patient. So how do we address that then, given that we are a lot of the times not so accurate in prognostication anyways?

Well, here is a general approach in discussing prognosis. And this approach is based on a SPIKEs pneumonic which is approach we use for breaking bad news as well. And we first start with the context. So identify first that the patient wants to talk about the prognosis, ideally sitting down in a quiet room, ideally with the patient’s family, with the patient’s permission and at eye level talking slowly and gently to the patient are important. Second, is a lot of the time it is
important to assess, what does the patient know? So simple questions such as, “What have your other doctors told you about your disease?” Or, “what is your understanding of your life expectancy?” are simple questions that we can ask. And patients a lot of the times can give us a pretty good idea what they think is going on. And this is important because a lot of the times it will help us set the stage. Let’s say you think a patient only has three months to live and the patient says that, “Well, I think the doctor --- last doctor told me that I only have a few months to live.” Well, then you --- you know that they already got pretty much good information and maybe you don’t need to go too far. But if they think that well the patient says that “I can live for a while and my doctor last told me that I can potentially be cured from this cancer for the next --- you know, with the next treatment. And I’m hoping to, you know, go to my granddaughter’s wedding in two years’ time,” then you know that there may be a little bit of a gap that you need to bridge before perhaps you provide the bad news. The third part is information, and particularly, how important this information is going to be to the patient. “Why do they want to know about their prognosis?” “How is it going to help them plan ahead?” Sometimes I ask them that question and they say, “Well, I want to make it to my, you know, son’s graduation from college which is going to happen in --- you know, in a few months’ time and I wonder if I can make it?” So these are very important personal decisions that it would be helpful if you can provide some guidance in that regard and help empower the patient. So this information can potentially be used a little bit later on. Then, it comes to the part of discussing the prognosis and when they do studies asking experienced oncologists how they discuss prognosis a lot of the times they emphasize that there’s a lot of uncertainty. That we really don’t know, and a lot of the times we’re actually wrong. And patients know that and they actually appreciate that we have some humanity in acknowledging that we are only humans and that they appreciate that information is not always correct. Then, it comes to talking about the actual prognosis. Well, rather than giving a specific number, we now recommend that let’s provide information in terms of hours or days or weeks or months or years. So let’s say I think a patient might have three months to live, while in my mind I may actually, you know, talk to the patient and say I think it is likely not in terms of days or weeks but maybe more in terms of a number of months and I think years will be fairly unlikely. So this information may be enough for patients to, you know, get a sense of control over their lives and at the same time allow us to give as accurate information as possible so that they can plan ahead without being wrong most of the time. So importantly, it’s important to use a language that patients understand. So if they focus, for example, on whether they can make it to their son’s graduation, well, maybe that would be saying you know I think there is a possibility, you know, that in --- in a number of months that you can make it to --- hopefully to the --- to the graduation although there is still some uncertainty ahead. And the patient could kind of take advantage of this information a little bit more. Importantly, I think when we give the information a lot of the times, the patients may cry. They you know have different emotions, such as anger. And it is important to respond to their emotion. In fact, this is an empathic opportunity where we need to acknowledge what they’re going through, you know. So a lot of the times simple statements such as, “Well this is a very difficult time for you and your family”. Or, “You know you have gone through a lot already”, and you know, simple statements to acknowledge them can be very important in establishing this relationship. And then, finally, I think it’s important to plan ahead and having a strategy would be important to make sure that we are not abandoning the patient, to make sure that we have a good follow-up plan. In fact, every prognostic discussion is an opportunity to empower the patient to plan ahead and to work towards improving their quality of life and quality of care. So if the patient and you still have the energy and time it would, may be a good opportunity to talk about advanced care planning if you haven’t done so already. Or, it could be a good opportunity to discuss why you do not recommend going for further chemotherapy. So these are very practical plans to help the patient move forward. On top of that, you know, there may be referrals that
could be helpful such as to social work, to Hospice, to Psychology that can be initiated at this point as well.

So just to clarify in the first part --- Part I and II of this talk, I was trying to give you all the information to make as accurate a prognosis as possible and hopefully get some ideas of the median ranges and numbers, whereas just now I said, that “Well you know when we talk to patients we don’t need to be, you know, very specific, just keep it general.” So that’s kind of a paradox in a way. But I would have to say that in a way both are true. In a way, we want to have accurate information and that is more to satisfy the clinicians’ needs to make sure that even if we are talking in general terms that we kind of know what we are doing and that we can give patients a good idea without being very far off range. And then, even if we know exactly by the minute when the patient is going to die, we need to still keep it as general as possible. Hours, weeks, days, these are very practical timeframes that can help the patients and family move forward without setting an expiration date for them.

So just to show you a little bit of literature in terms of how important prognostication understanding is for patients and family, here is one study asking patients to estimate their chances of survival in the next six months. And if the patients think that they have a low chance of surviving past six months, they also have a much lower proportion of them choosing to go on life-extending therapy. So there are practical implications in terms of a good prognostic understanding.

And finally, I’d like to talk about one study in terms of how, perhaps, palliative care can help with this process. So in addition to you know oncologists or primary care physicians talking to patients, the palliative care team may actually be a good tool sometimes if you find these discussions difficult to perhaps work with the patients and focus on communicating and making some decisions around prognosis as well. So this is a randomized controlled trial looking at 151 cancer patients with advanced lung cancer and from within two months of their diagnosis, they were either referred to a palliative care outpatient clinic or routine oncologic care and their primary outcome was quality of life.

And those who are referred to palliative care regardless of their distress level, they tend to have better quality of life, lower rates of depression, better end of life care outcomes, and better documentation of their resuscitation status.

But also, very interesting is that those patients referred to early palliative care also live longer. But that is not the key point that I want to talk about today for this presentation.

But rather, I want to show you that those in a sub-study but belonging to this randomized trial, those patients randomized to early palliative care in blue here, they also were able to have a better and more accurate understanding of their prognosis over time as compared to patients who [are] receiving standard oncologic care and the majority of these patients did not get a palliative care referral. So palliative care seems to maybe have an impact on those patients to a certain extent.

But on top of that, the interesting thing is that among patients who are referred to the palliative care arm and those who are able to have an accurate prognostic understanding, they have a much lower rate of receiving chemotherapy at the end of life as compared to patients who don’t understand their prognosis. So that kind of makes sense, but this is in contrast to the patients who have been randomized into oncologic care. I mean I am not showing the graphs with that arm here but essentially,, regardless of whether they have an accurate or inaccurate prognostic
understanding their rates of getting chemotherapy in the end of life is about the same. There is no difference. So what this means to me is that perhaps palliative care not only helps patients to have an improved understanding of their prognosis, but also take advantage of this information to make plans ahead including avoiding some aggressive measures at the end of life. And this is encouraging. Keeping in mind this is only a small study and we --- we do need further evidence down the road.

So just to summarize then, in Part I, II, and III of this talk on Prognostication for Advanced Diseases, our take-home messages would be that clinicians tend to overestimate survival based on the clinician prediction of survival. And we can rely on many prognostic factors that can help us improve our accuracy to a certain extent. The most important one perhaps is the performance status and that applies not only for cancer patients, but patients with other diseases as well. And other important prognostic factors include poor nutrition, advanced age, and significant comorbidities. There are already multiple prognostic models available to help us improve our ability to prognosticate and in fact patients want to know about their prognosis. And we should explore the timing of when we want to talk to them and most importantly take advantage of these opportunities to empower them and to help them to plan ahead. So this is a very important take-home message here, to utilize this information to help them focus on hope. And this concludes my presentation and we welcome any feedback or comments. Thank you.