Okay, I am Dr. David Hui from the Department of Palliative Care from The University of Texas MD Anderson Cancer Center and we are going to talk about Prognostication in Advanced Diseases, Part II.

So in the first part, I touched on some prognostication principles for patients who have advanced cancer and now we are going to talk about patients who do not have cancer, but have other advanced diseases.

Now there are quite a few advanced diseases out there and just to be very organized we will talk about some of the cardiopulmonary diseases, such as COPD and heart failure. We will touch on hepatic and renal failure and also some neuromuscular diseases. And for each of them, we will talk about the prognostic factors that are established in the literature, some of the prognostic models that are available, and also the hospice referral criteria for these patients.

Before we go into each one, I just want to highlight that the disease trajectories for each of these categories are a little bit different. As I mentioned in part one, for cancer patients they tend to have a slow decline and then there is a rapid cliff going downwards. But for COPD and heart failure patients, their trajectory fluctuates a lot more and sometimes they have an exacerbation ending up in the hospital or even the intensive care units. And they may come very close to even dying and you don’t know whether they can actually come out alive or if they’re just going to die in that particular admission. So it becomes even more difficult to predict their survival. For patients with dementia and stroke, they usually have a poor functional baseline to begin with and then there is a progressive decline over time. And for other diseases, such as hepatic and renal failure, depending on the disease management, these patients may have a progressive declining course, but starting out from a higher baseline.

So we mentioned earlier that for cancer patients, clinician prediction of survival is not very accurate. But the interesting thing is that for the other diseases, particularly COPD and heart failure, it is even less accurate. So here is one study. They look at how clinicians predict survival by eyeballing patients. And they asked the clinicians to estimate how long their patients would live and then look for the percentage of patients in which they actually died in six months, but the clinician provided an estimate of more than a year, so, at least two folds over estimation and by six months which is quite a large difference. And this is what we call a significant prognostic error. So for cancer patients, well, partly because we have some good understanding of the prognostic factors and the trajectory, this only happens in 10% of the cases. But for COPD and heart failure patients a serious prognostic error happens in 60-70% of patients. And so you might as well flip a coin in deciding than asking a doctor to predict whether this patient will live for six months or longer.

So let’s go through each disease then and understand some of the established prognostic factors starting with COPD.

Well, for COPD the main prognostic factors are lung function indicated by FEV1. And if you have an FEV1 of less than 35%, then this two-year survival is only 75% and the four year survival is about 45%. The other important variables that you actually see over and over again in all the disease groups would be patients who are older, those who have nutritional failure as well as functional status --- a poor performance status. And these are the variables that can also help us decide that the patient is not going to do well. So I typically think of a frail old man who is maybe thin with a significant amount of obstruction and you know not very functional and those are the individuals who have a poor prognosis.
There are some prognostic models out there. The most established one is the BODE Index, B-O-D-E. And it consists of basically the weight loss as well as significant airway obstruction, decreased function in terms of walking as well as a significant degree of dyspnea.

And if you add up the total score, then again the higher the score the worse the prognosis. The important thing to understand in this score is that it’s still very hard to differentiate people who have a very short survival. Because even in the highest prognostic scoring group, there is only a 5% one year mortality for these patients. So perhaps it would be helpful to understand in this group of patients whether further variables can help differentiate their survival.

But there has been some work also done to look for patients who are admitted to the hospital and those are the patients who tend to do not as well and looking at some of variables that can differentiate who is going to do well and be discharged from the hospital versus who are going to die in the hospital. And basically, patients who have multiple episodes of mechanical ventilation or significant prolonged periods of requiring a ventilator, significant comorbidities, hypercapnia, as well as nutritional issues are the ones who tend not to do well, which makes sense.

And in addition to COPD, I would say that another obstructive disease, cystic fibrosis, also has many similar prognostic factors. This disease used to be one in which people lived to their 20s and then nowadays with the technology people are living, you know, mostly above the 40-year mark and hopefully this will continue to increase. But still these patients die early and the factors that predict that include FEV1, again obstruction, hypercapnia, and also nutritional failure, if they need a nutritional intervention. Interestingly, technology can help because if they are referred to an accredited cystic fibrosis center with a, you know, very comprehensive team they tend to do a little bit better in terms of their survival. And of course as they get diagnosed later and later they also do better as well.

In regard to the hospice admission criteria for pulmonary diseases, the key indicator is that patients should have chronic progressive pulmonary diseases with dyspnea at rest. So this is the mandatory criteria. On top of that, they should have one of the two meaning either hypoxemia or hypercapnia. So that would fulfill the criteria for admission to hospice.

And, then, there are a number of supportive criteria that are also prognostic but are not required for the patient to have before they enroll.

Keeping in mind that these variables are established more by expert committees and in fact, when they actually look at how well these criteria predict a six-month survival or less they tend not to do very well. So I think a lot more work is actually needed to address that, but in the meantime these other criteria that are established and accepted by our healthcare system.

Now, the next category would be multisystem organ failure…

…and particularly talking about patients who require intensive care. One of the most common diagnoses would be sepsis. And this is a disease that not only has a very significant short-term mortality. But also even in the longer term, even if patients recover from the sepsis, you know, at a one year mark 72% of them will have died. And part of the reason is because patients who have sepsis a lot of the time have significant comorbidities and diseases that put them at risk and with compromised immune systems a lot of the times and they may also die from the other chronic diseases as well. In the ICU setting, we are particularly interested to know whether the
patient will be able to be discharged alive ultimately from the hospital. And there are some
prognostic models available. The most well-established is the APACHE system which has
multiple generations and now comes down to APACHE IV.

The second generation had 12 variables…

…but in the 4th model it now has…

...up to 140 mo --- over 140 variables including many vital signs both on admission as well as
part way into the hospital stay. And you need to enter a lot of the comorbid conditions as well.
And it gives you information not only of in-hospital mortality, but also the predictive length of
stay for those patients. And this could be useful for benchmarking and quality improvement
purposes in addition to predicting patient survival. There are also a number of other prognostic
scoring systems like the MPM and this one, for example, only has 16 variables and it gives you
a little bit less information focusing mostly on in-hospital mortality. So which model to use is
partly depending on the institution and the setting.

So the next category would be heart failure.

And this is actually a fairly deadly disease. For patients who have stage IV or class IV heart
failure indicated by dyspnea at rest their median survival is only in terms of maybe eight months
or so and the one year survival is 30-40%. So these patients have a very poor prognosis. In
fact, you could argue worse than some of the patients with metastatic cancer.

And other than the New York Heart Association being the key prognostic variable, there are
many other things indicating, for example, cardiac function, relative arrhythmia, or the ejection
fraction can be prognostic. And again, the patient's nutritional status as well as the
comorbidities are some of the key variables that can help predict how they are going to do.
There are also a number of laboratory variables, such as hyponatremia, renal failure, as well as
anemia that can give some information as well.

Taking into account, many of these prognostic variables, both demographics as well as their
cardiac function, comorbidities, there is the Seattle Heart Failure Model. And I would invite you
to visit this website to take a look. And this model not only includes the well-established
prognostic factors, but also has an option for you to enter whether the patient is receiving
medical therapy such as beta blockers or ACE inhibitors. And based on that gives you an
estimation of how much treatment is modifying prognosis. So it’s a good website to look at and
very informative.

For patients who have been hospitalized with decompensated heart failure, these patients
obviously have a particularly worse prognosis. There has been a study looking at some of the
variables that can differentiate who is going to be discharged alive versus those who are going
to die in the hospital. And based on three variables, if they have a very high urea level, a low
systolic blood pressure as well as high creatinine, then this group of patients has a 20% chance
of in-hospital mortality.

So hospice admission criteria is straightforward. It’s just the New York Heart Association Class
IV meaning dyspnea at rest and on top of that they should be medically optimized.

All of the other prognostic variables that we talked about are supportive in nature and are not
absolutely necessary for patients to be admitted to hospice.
The next disease now is chronic kidney disease.

And this in particular we are focusing on the WHO Stage 5 disease meaning those who have creatinine clearance of less than 15 cc/min. And this is the category of patients we used to call having end stage renal failure. For these patients, they a lot of the times may have to make the decision whether to go on dialysis or not. And these are the patients who do have fairly advanced disease with a short survival. Their life expectancy is about a quarter of those who do not have renal disease and the median survival is only 2.5 years. And this is what I call the 25% category disease because many of the things can be easily remembered with about 25%, such as you know their rate of mortality rate per year while they are on dialysis is about 25%. So one in four patients would die after a year. And then, for the patients who die while they are on dialysis about a quarter of them actually decide to stop their dialysis before they die and once they stop their dialysis for those who have dialysis dependence, their median survival is only about two times five which is about 10 days. So this is a fairly short number and one that sometimes patients would actually like to know.

So what are the prognostic factors then, other than knowing that they all have stage 5 chronic kidney disease? Well, once again the same variables that came up before in other diseases are significant including if you have older age, multiple comorbidities, poor physical function, poor nutrition. These are all associated with a short-term survival.

And there is a prognostic model on a website available incorporating some of these comorbidities, age, and albumin level as well as a clinician prediction of survival question. And by entering this, you will be able to get an estimate of the patient’s prognosis in the short term.

Hospice admission criteria include essentially the fact that patients have significantly impaired renal function with a creatinine clearance less than 10 cc/min or serum creatinine greater than 8. And they have to decide not to go on dialysis, if they are eligible for dialysis. Or if they are already on dialysis, they have to, you know, discontinue it. And they should also have some signs and symptoms of significant renal failure as indicated by the list here, such as hyperkalemia or hepatorenal syndrome. Once again, these are prognostic as well.

There are some supportive criteria that we mentioned earlier, but these are not mandatory for the hospice admission.

The next disease we would like to talk about is chronic liver disease.

And for some patients who have hepatitis or other types of liver disease, they can go on for a long time, for many years. But those who have decompensated liver failure meaning those who have significant symptom burden, elevated bilirubin, ascites, hepatorenal syndrome, or evidence of coagulopathy, meaning functional of the liver, they tend to have a much shorter survival with a median of about two years. So the well-known prognostic factors, again, not only includes the liver function markers, but also if you have comorbidities such as hepatocellular carcinoma and age once again is important.

So the prognostic model that has been developed for this disease, the one that we use nowadays is the MELD’s model and this --- there are multiple versions of it with the original version, the UNOS version, as well as the sodium version. But all of them essentially incorporate creatinine, bilirubin, as well as INR and based on these numbers you come up with a total score and the higher the score the worse the prognosis.
So you can see here, for example, patients who fall in the highest scoring category they are estimated by the models to have a 90-day probability of death of about 80%. And you know, they do indeed because the actual survival is only about 65% or so. So there is some good --- reasonable correlation, but not perfect sc --- concordance in regard to the prediction.

For hospice admission criteria, once again, it is the organ function that is in the first category. So they have to have an INR that is elevated as well as hypoalbuminemia indicating liver dysfunction. And they should have some criteria clinically suggesting that they are in the decompensated state with ascites, bacterial peritonitis, varices, or hepatorenal syndrome among others and they are not going for liver transplant. So if they fulfill these two criteria, then they will be eligible for hospice.

Again, the rest are supportive in nature at this time.

Moving along, take a big breath, and it's the next disease, HIV.

So HIV used to be a highly life-threatening disease, but with the invention of HAART therapy, this disease, people tend to live longer on it. But at the same time, many patients will still die with AIDS. So AIDS is defined as CD4 count less than 200 or if you had any of the AIDS-defining illnesses as indicated here.

And it is absolutely true that patients live for longer after the invention of the HAART regimen with the multiple anti-retroviral therapy. At the same time, the disease indicators such as CD4 count for HIV is still highly prognostic. So patients who have a very low CD4 count they tend to have some more shorter survival compared to those who have a higher CD4 count presentation.

And in fact, another very important marker of disease activity is the viral load.

And so, one analogy that I have for prognosis using the viral load and the CD4 count is imagining a train that is going to hit a wall and is traveling at high speeds and how much track before you hit the wall is essentially the CD4 count and how fast the train is going is the viral load. So the lower the scans, the higher the viral load, the shorter the prognosis.

And in fact, there is a website that includes not only these two prognostic factors but other established factors such as age, clinical stage, admitting symptoms at presentation as well as comorbidities, such as IV drug use because they can also have a huge impact on patient’s mortality and then give us the 1, 2, 3, and 4 year estimation of the patient’s probability of survival.

So here is just an example based on some numbers that we enter. And they can give us a pretty good estimate with 95% competence interval.

So hospice admission criteria fairly straightforward. Once again, you need some marker of disease severity and that includes CD4 count that is very low or viral loads over 100,000 copies. And you need to have some life-limiting complications from the HIV and many of them are AIDS-defining illnesses essentially.
And then, you also need to have a decreased performance status so this is an important factor. The other criteria listed here in 5 are supportive in nature.

So moving along to the next category of diseases would be the neurological disorders and first we’ll talk about ALS.

This is a neuromuscular disease and patients have a median survival of about three to five years and a small percentage do live for a longer term. So the key prognostic factors here are -- are once again related to how aggressive this neuromuscular disorder is affecting the patient. Many of them may die because of their poor function. They may die because of nutritional failure as well as respiratory failure. So function rather is related to the pulmonary aspect or the nutritional aspect is very important and incorporated in some of the functional scales that I will show you in the next slides. Other important prognostic factors include the fact that if they have more brainstem involvement rather than limb involvement and whether they have a older age as well as the duration of symptoms prior to presentation.

So here is the ALS functional rating scale which incorporates 12 domains that essentially measures the activities of daily living but also monitors their pulmonary function as I mentioned earlier and to a certain extent the ability to feed themselves and swallow. And for each of the items, you give a score and you add up the total score and the higher the score the worse the prognosis and the higher the risk that they will need tracheostomy.

So hospice criteria requires that patients have evidence of rapidly progressive ALS indicated by, you know, essentially any of these criteria listed below

But also one of the three categories listed here to augment the admission. So you have to have either respiratory failure or nutritional failure

Or you have to have significant complications, such as repeated urinary tract infection, decubitus ulcer because patients are bed-bound, recurrent aspiration pneumonias, or many of the infectious complications because patients are immobile, they are immunosuppressed, and they are at risk for many of these life-threatening events.

Dementia is the next topic to address.

And in the past, we think of dementia and people living with it for maybe decades but a study in the New England Journal came out and suggests that patients who have Alzheimer’s or vascular dementia, two of the more common types of pathophysiology contributing to dementia, actually have a fairly short median survival only in terms of about three years. And the reason why they were able to support that is because they are saying in the past when we look at dementia, we tend to capture data on people who have maybe more indolent disease. And when we actually also include patients who have dementia and die very rapidly which we tend not to classify them as having dementia, then we actually adjust the average to be a lot lower than what we thought it would be before.

So this is what they propose in terms of a few years and once again the key prognostic factor here is related to patient function, so...

…if they have difficulty ambulating/walking. So this essentially equates to ECOG performance status 4 for cancer patients then they suggest that they have a fairly poor function and that their prognosis is limited and this stage 7C is in fact the one that we use for hospice admission
criteria. And beyond that, those patients tend to have even more difficulty even sitting up. They eventually lose the ability to smile or even get their heads up and you can see these are major, major limitations. These patients have very limited quality of life, have significant difficulty looking after themselves in any way, and are completely dependent on care. So they not only have a poor quality of life, but also quantity of life.

So other than functional status, as we mentioned, if you have multiple complications that would not help the prognosis, again old age and mental status also contribute to it as well.

There has been a prognostic model looking at the patients who have dementia in the nursing home setting and predicting their survival. And here are some of the factors that you can assess and then enter into the scoring system and essentially the higher the score the worse their survival. So for instance, patients who have a score of 12 or more, they have a 70% chance of dying within the next six months.

Hospice admission criteria as I mentioned is really dependent on the stage 7c meaning that they cannot ambulate without assistance.

But also patients who have evidence of medical complications similar to the ALS category. So, that a lot of them are infections that are recurrent as well as nutritional impairment meaning difficulty swallowing or significant weight loss.

Moving to the next category is stroke and coma.

So in contrast to dementia, stroke can be sometimes very acute and it is actually sometimes difficult to estimate their prognosis. But there are four categories listed by the hospice admission criteria that if patients with acute stroke fulfill any of them they would be potential candidates for enrollment into hospice. And they include patients who have significant duration of coma or persistent vegetative state beyond three days after an acute stroke, if they have severe myoclonus or obtundation beyond three days, or if they have abnormal brain stem reflexes on day three of the coma. So by day three pretty much, you get a very good idea what is going to happen to the patient and if they have any of these persistent coma or vegetative states or abnormal neurological signs that are significant then it essentially predicts a poor outcome and they may qualify for hospice.

Those who are not able to eat at all after an acute stroke will also qualify for hospice as well if they are not a candidate for artificial nutrition. And then CT and MRI findings are supportive only.

And for patients who have chronic stroke and this is a different category, they actually recover partly from their stroke, but they still have very poor baseline. Who would be eligible for hospice? Well, this is kind of similar to the failure to thrive category for Hospice admission as well. Essentially they have to have a Karnofsky Performance Status of 50% or less and on top of that have some evidence of nutritional failure indicated by significant weight loss or albumin that is very low.

And if they have other things, such as medical complications that, again, is supportive in nature.

So in part one and part two, I have discussed a lot of different diseases and some of the prognostic factors. And this slide is meant to kind of put them all together for an overview anywhere from cancer all the way to stroke and dementia. And they have different trajectories
in terms of the patient function. They have somewhat different median survival but all of them indicate that the patient has a limited prognosis. But importantly the key prognostic factors seem to be very similar regardless of disease type. If patients have a poor performance status, they tend not to do well. If they have significant nutritional failure, they tend not to do well. If they have advanced age and comorbidities, they also tend not to do well. Of course, for the you --- specific organs such as heart failure or pulmonary failure or renal ki --- liver failure you have to also look at the individual organ function as well. And here is a list of some of the prognostic models that are available. Many of them are on websites for us to perhaps estimate the prognosis a little bit more. This concludes the second part of this presentation and we will welcome any feedback or comments. Thank you.