[MUSIC PLAYING]

DHIRAJ YADAV: Good morning. My name is Dhiraj Yadav. I'm a professor of medicine in the Division of gastroenterology, hepatology, and nutrition at UPMC. I wanted to thank the course directors for inviting me to talk to you this morning about an update in the management of pancreatitis.

I've organized my presentation into two sections. In the first, I'll talk about acute, and in the second half I'll talk about chronic pancreatitis. In each of those, I will discuss some core concepts about the disease and then will also touch upon some latest developments in the field. I do not have any conflicts to disclose.

I'll start with the case of a 52-year-old female who was admitted with sudden onset of right upper quadrant and epigastric pain, nausea, and vomiting. Her vital signs are significant for mild tachycardia. Physical exam is remarkable for tenderness in the right upper quadrant and epigastrium. Her laboratory tests are significant for elevations in transaminases, and her total bilirubin is 4.6. Her lipase is elevated multiple folds to 494.

Her ultrasound and CT scan show evidence of gallstones, thickened gallbladder wall, pericholecystic fluid, evidence of mild pancreatitis with peripancreatic inflammatory changes, and no pancreatic necrosis. Because of the dilated common bile duct and abnormal liver function tests, she underwent an MRCP that shows possible sludge and a stone in the distal common bile duct.

This case brings out several management issues in patients with acute pancreatitis that I'll review with you, including assessment of severity of acute pancreatitis, what should be the workup for etiology of acute pancreatitis, the role of ERCP and timing of cholecystectomy, and then what to expect in terms of natural course after recovery.

Now the incidence of acute pancreatitis has been steadily increasing in the past 4 to 5 decades. In the US, the yearly incidence is 40 to 80 cases per 100,000 per year, which translates to over 250,000 cases each year for hospitalizations. This makes acute pancreatitis among the top GI causes for hospital admission.

In a recent meta analysis that evaluated temporal trends in acute pancreatitis around the globe, what was noted is from the countries where the incidence was reported, in the brown and the yellow colors you see the countries where the incidence is increasing.

Looking at the data in a different way, in these two panels on the y-axis is incidence of acute pancreatitis, and on the x-axis is year. In the top panel in each of the continents and in the bottom panel is stratified based on etiology-- biliary or alcohol-- you can see that there is a general increase in the incidence of the disease.

In terms of the causes of increase in acute pancreatitis-- for biliary pancreatitis-- because obesity is increasing in the general population. Obesity is a risk factor for gallstones, and that is the most common risk factor for pancreatitis. In terms of alcohol consumption, there has been an increase in alcohol consumption in different populations which accounts for increase in alcoholic pancreatitis.

For diagnosis of acute pancreatitis, we require two out of the three features-- that is characteristic upper abdominal pain, which is typically sudden in onset, elevation of serum pancreatic enzymes to three, or more than three, times the upper limit of normal, and imaging evidence of acute pancreatitis or its complications. Understanding the disease severity is important because it can provide us an anticipation as to what to expect during the clinical course and also make treatment decisions.

Surrogate measures like SIRS, renal dysfunction, and hemoconcentration can give you an indirect idea about severity of the disease. In 2013, the revised Atlanta Classification was proposed based on new knowledge on the role of organ failure and necrosis on the clinical course of disease. And based on that, the disease can be stratified into mild, moderate, and severe.

Mild acute pancreatitis is when you have no organ failure and no local or systemic complications, that is necrosis or related complications. Moderately severe acute pancreatitis is when you have either transient organ failure-- that is organ failure lasting for less than 48 hours-- or presence of necrosis, or both. Severe acute pancreatitis is when you have persistent organ failure-- that is organ failure lasting for more than 48 hours.

It is important to recognize that organ failure and pancreatic necrosis typically go hand in hand. Or, in other words, the large majority of patients who have organ failure have underlying pancreatic necrosis, and about 50% to 60% of patients with pancreatic necrosis have organ failure. Presence of organ failure, necrosis, which is typically infected, is the situation where the mortality can be very high.

Going into a little bit more detail about necrotizing pancreatitis-- not that I would want you all to go down and look at all the CT scans, but for a conceptual understanding-- 80% to 85% of patients have mild acute pancreatitis, or interstitial pancreatitis if a CT scan is done with contrast.

As you can see here, either the pancreas may look completely normal, or it may look enlarged with inflammatory changes around that is seen here in green arrows. These patients typically have a short clinical course. Patients start to feel better by day two or three, and they are usually out of the hospital by day four or five.

Necrotizing pancreatitis occurs in about 15% to 20% of patients, and the three panels that you see here is evolution of disease at different stages. In the first panel is very acute in the course of necrotizing pancreatitis. The second panel shows what we call as acute necrotic collection, which is evolution over the next two to four weeks.

And then walled off necrosis, which is typically occurs after four weeks of illness when the necrotic area becomes more defined and has a wall. Understanding this is important because some of the treatment decisions in terms of percutaneous drainage, endoscopic drainage, or surgical treatment we typically try to reserve for beyond four weeks as much as possible unless the clinical course is deteriorating.

In terms of etiology of acute pancreatitis, gallstone is the most common cause of acute pancreatitis followed by heavy alcohol consumption, typically in association with smoking. Other important causes are hypertiglycerdemia, medications, and uncommon causes like post-ERCP pancreatitis, trauma, hypercalcemia, and major upper abdominal surgery.

In a specific group of people-- usually individuals who are more than 50 years of age and who do not have traditional risk factors-- pancreatic cancer is something to consider, and it can present as acute pancreatitis as initial manifestation. Certain autoimmune disease, like celiac disease, increases the risk of pancreatitis. In autoimmune pancreatitis, a subset of these patients can present with acute pancreatitis.

If no obvious etiology is identified, then we term it as idiopathic. When patients typically have recurrent attacks then further evaluation is performed that could uncover pancreatic ductal abnormalities like pancreas divisum or genetic factors.

In terms of workup for first attack of acute pancreatitis, the American Pancreatic Association recommends that the minimum workup should include-- in addition to a good history-- liver function test assessment, because it can give you a clue towards biliary etiology if the LFTs are elevated, especially if they are more than three times the upper limit of normal.

Abdominal ultrasound, again, can give us the status of the gallbladder in terms of stones, and also assess the common bile duct. Serum triglycerides should be performed as early as possible after admission because delaying estimation could lead to false normalization and you can miss the diagnosis. Calcium is typically included in all metabolic panels.

I include CT scan here not to suggest that it should be done in all patients, but that 70% to 89% of patients in the US who have acute pancreatitis have CT scan during their clinical course. It is not usually helpful to identify the etiology. In patients who have no etiology uncovered, we typically do a celiac panel even after the first attack, and in a select group of patients who have morphology that is suggestive, we do a serum IgG4.

I include a pet level here, not as a recommendation, but in a small subset of patients where there is clinical suspicion a pet level can give you an idea about alcohol consumption even two to three weeks before the test is performed. But this should be performed after discussion with the patient.

If a patient has idiopathic pancreatitis, like I mentioned, in a correct setting, the an endoscopic ultrasound could help us to uncover a small pancreatic cancer. Or if a patient has recurrent pancreatitis, then an MRI MRCP, typically with secretin, can help to assess for ductal abnormalities.

And then endoscopic ultrasound can also help us to know about sludge in the gallbladder or subtle changes of chronic pancreatitis. Many genetic factors can now be commercially tested through different labs.

I also want to touch upon briefly about hypertriglyceridemic pancreatitis, which is an entity that is typically under-recognized and under-diagnosed The most common clinical scenario where you will come across a patient with hypertriglyceridemic pancreatitis is somebody who has poorly controlled diabetes who does not have traditional risk factors. The other situation will be an alcoholic pancreatitis patient who has hypertriglyceridemia.

Third would be certain medications that can increase triglyceride level, like beta blocker, thiazides, propofol, certain HIV medications, and others. And then third-trimester of pregnancy. The common scenario here is that these are secondary risk factors. And when they are present in an individual who has predisposition to hypertriglyceridemia, which now is believed to be a polygenic trait, their triglyceride levels can go high-- typically more than 1,000-- and a subset of those patients can have pancreatitis.

Other thing to remember is that hypertriglyceridemia is also an independent risk factor for disease severity. These are data from a large international registry where patients who had triglycerides performed in the first 48 hours. They looked at the odds of severe acute pancreatitis in these patients, and a dose-dependent association was noted with odds of as high as nine-fold greater.

Another thing to remember is that patients who have hyperlipidemic pancreatitis, the risk of recurrences in these patients can be significantly reduced by controlling the secondary risk factor. For example, controlling diabetes, avoiding alcohol consumption, adequate diet and lifestyle changes, and medication use.

These are data from Kaiser Permanente that showed that patients in whom triglycerides were better controlled after discharge, these patients had significantly lower risk of recurrent acute pancreatitis as those who had moderately elevated or highly elevated triglyceride levels.

Our patient had sludge and stone in the distal common bile duct. This is a situation where an ERCP, typically before cholecystectomy, is helpful to clear the common bile duct. The other indication of ERCP would be a patient who has evidence of cholangitis or suspicion of cholangitis. Now, in terms of cholecystectomy, this should be performed as soon as possible after an episode of acute pancreatitis, preferably during the same hospital admission.

The data I show you here is from a multicenter randomized clinical trial from the Dutch Pancreatitis Study Group where patients were randomized to either received same admission cholecystectomy or interval cholecystectomy. What was shown is that same admission cholecystectomy led to a 75% reduction in the risk of the primary composite outcome of mortality or gallstone related complications or recurrent pancreatitis.

Now what to expect in terms of the natural course of acute pancreatitis after discharge-- what we are learning is that acute recurrent acute and chronic pancreatitis represents a disease continuum. The risk of recurrence is based on what was the primary etiology. So in other words, in conditions like gallstone related pancreatitis or triglycerides or medication the risk can be substantially reduced if you address the primary etiology.

In alcoholic pancreatitis or idiopathic pancreatitis, the risk of recurrence is greater, but even in patients with alcoholic pancreatitis, the risk can be significantly reduced from abstinence from alcohol typically along with cutting down on smoking.

Now, we initially discuss about necrotizing pancreatitis. In these patients, especially if you have significant amount of necrosis, one would expect that in addition to the exocrine pancreas, the beta cells can also be affected, or loss of beta cells will be there, which could put them at risk for diabetes.

But what about a patient who has mild acute pancreatitis like our patient that we discussed at the beginning? Are these patients also at an increased risk for diabetes?

Well, until a few years ago, this was not something on our radar. A meta analysis in 2014 showed that patients who have acute pancreatitis, they are at high risk for diabetes in the next three to five years. Even patients with mild acute pancreatitis are at an increased risk.

What was also noted is that a significant fraction of these patients need insulin treatment-- much more than what you would expect-- than in patients with type 2 diabetes. There are a couple of population based studies that have subsequently shown that the risk of diabetes after mild acute pancreatitis is increased about two-fold as compared to age and sex matched controls.

A recent prospective study from New Zealand in 152 patients, mostly with mild acute pancreatitis, assessed diabetes status at six month interval for about two years by performing glycemic parameters. And what the investigators found was that the risk of diabetes was 11% at two years. And the risk of pre-diabetes was as high as 45% in these patients, increasing their probably of diabetes subsequently.

The other way to look at the burden of acute pancreatitis on diabetes is if you look at all diabetes patients, about 1.5% to 2% of those are type 1 diabetes and approximately 2% are related to diabetes from the exocrine pancreas. Among patients who have diabetes relating to the exocrine pancreas, about 60% to 70% are related to either acute or chronic pancreatitis and the rest are from pancreas cancer, cystic fibrosis, and other uncommon causes.

Among all patients who have diabetes relating to pancreatitis, about 60% to 70% are due to acute pancreatitis, in contrast to what we typically believe, that diabetes is more common with chronic. This is because the incidence of acute pancreatitis is about eight to 10-fold greater than chronic pancreatitis. And even a modest increase in the risk of diabetes increases the total burden of disease from acute pancreatitis.

There are also clinical implications of diabetes after pancreatitis. The data that I show here are from two population based analysis. On the left is from United Kingdom, and on the right side is from Denmark. Investigators identified all patients with new onset diabetes and followed these patients to determine the need for insulin treatment.

As compared to patients with type 2 diabetes-- which is shown in the blue line on the life and the bottom line on the right, the dotted line-- patients who have diabetes either after acute or chronic pancreatitis had about a three-fold increase in the need for insulin during longitudinal follow up. And the glycemic control in these patients was worse as compared to patients with type 2 diabetes.

Now, there are a lot of unanswered questions in this area in terms of what are the patient and disease related factors that account for diabetes or increase the risk of diabetes. What happens to beta cell function, insulin resistance, and other factors? What is the role of immunity in development of diabetes in these patients?

So recognizing these knowledge gaps, the NIDDK established a consortium called Type 1 Diabetes in Acute Pancreatitis Consortium in 2020 to investigate this. The members of the consortium have assembled a longitudinal observational study called DREAM, or Diabetes Related to Acute Pancreatitis and its Mechanism, which was launced earlier this year.

The consortium consists of 10 clinical centers and one data coordinating center. The specific aims of DREAM project is, number one, to determine the cumulative incidence and clinical characteristics associated with the development of diabetes after acute pancreatitis.

Second is to comprehensively characterize beta cell function and endocrine alterations in these patients and its relationship to diabetes after acute pancreatitis. And last is to assess for immunologic mechanisms of diabetes after acute pancreatitis, including beta cell autoimmunity.

The project proposes to enroll 1,000 patients with acute pancreatitis over a three year period of whom 800 would have no pre-existing diabetes. These patients are going to be carefully followed at different time points starting at three months, six months, 12 months, 18 months, 24 months, and yearly thereafter.

At which time, they will get assessment for diabetes at each time point, they will undergo deep metabolic phenotyping, they will get immunologic studies. A subset of these patients are going to get research MRIs to assess for morphologic changes that associate with diabetes, and a biorepositiory is also going to be established. Hopefully, in the next three to five years we are going to be able to answer many of these questions.

So to summarize the acute pancreatitis part of my talk, determining the severity of acute pancreatitis is important to anticipate the clinical course. Establishing etiology provides the best chance to prevent disease recurrences. Serum triglycerides should be assessed as close to admission as possible.

Patients with mild gallstone related acute pancreatitis should undergo early cholecystectomy. And even mild acute pancreatitis increases the risk of subsequent diabetes.

Moving to chronic pancreatitis. Again, I'll start with a case that outlines some of the challenges in management of these patients, which I'm sure that you come across in your daily practices. This is a 38-year-old male with past medical history of bipolar disorder. He had four episodes of acute pancreatitis between 2016 to 18. Unfortunately, he has developed chronic pain, which is present most days of the month.

He takes a lot of Tylenol and Motrin and tries to avoid opioids. His diabetes was diagnosed around the time of his first attack of pancreatitis, and he's on high doses of insulin. He has also lost about 50 pounds over the past year and has clinical signs of steatorrhea. He has never been a heavy drinker but he does smoke. His etiologic workup was negative including genetic testing.

The CT scans that you see on the right side show calcified chronic pancreatitis with disease that is dominant in the head of the pancreas obstructing the pancreas duct and resulting in pancreatic ductal dilatation.

Challenges in management of this patient include what should be the optimal management of pain for this patient? Will this have a durable response? Are there adjunctive treatments that could also be performed that could improve pain management or response to therapy in these patients? Can you predict if this patient undergoes invasive therapy, will that be helpful? And then, I will also discuss about a couple of sequlae of chronic pancreatitis.

So chronic pancreatitis has a profound effect on quality of life of these patients. These are data from more than 1,000 patients who are part of the NAPS2 study, which is a multicenter cross-sectional US study that has contributed to a lot of our learning in the last 15 years.

In the left panel is physical quality of life, and the right is mental quality of life. What you see in the star is the bar graph showing the contribution of pain, which is the single most important factor resulting in decrement in quality of life in these patients.

Over the course of chronic pancreatitis, 90% of patients have pain at some point of time. If you look at it in a cross-sectional manner-- again, from the NAPS2 data-- 2/3 of patients report that they had severe pain at some time in the past year, and about 55% report that they had constant pain in the past year. About half of the patients are taking narcotic medication at any given point of time.

If you look at the natural course of pain over time, these are very nice data-- again, from the Dutch group-- where patients were asked about their pain experience on a yearly basis. And during a median follow up of about 40 years, the investigators noted that there was frequent change in the type and pattern of pain patients had irrespective of whatever treatments that they received.

So when we see a patient with chronic pancreatitis who has pain, the first thing we do is a cross-sectional imagining study and additional evaluation to look for whether there are other factors that can explain pain. For example, local complications like a pseudocyst, pancreas cancer, whether the patient has a peptic ulcer that could explain pain.

If we do not see that, then initial trial of conservative management where behavior modification-- for example, cutting down on alcohol or smoking or other adjunctive treatments like pancreatic enzyme treatment-- could be tried to better assess the burden of disease.

After that, if a patient has obstructive disease-- that means blockage of the pancreas duct from stones or strictures-- endoscopic therapy is usually the first treatment to offer to these patients. And in a subset of patients, surgery could be considered. Patients who do not have duct dilatation, they are managed medically. In a small subset of selected patients, total pancreatectomy with islet autotransplantation is offered.

The problem is whether these treatments result in durable pain relief. These are data from a very recent randomized clinical trial from the Dutch group where patients who had chronic pancreatitis very early in their clinical course-- before they became narcotic dependent-- they were randomized to either receive endoscopic decompression of the pancreas duct or surgery.

And they were carefully followed over an 18 month period. The primary conclusion of the study was that surgery does better than endoscopic therapy, but careful evaluation of data shows that patients who had endoscopic treatment and full clearance of the pancreas duct had a similar response.

But what I would like to highlight here are two points. If you look at the table and then graph on the right side, durable pain relief was achieved in less than 50% of patients. Which actually highlights the limitations that we have in terms of number one, durable pain relief with even aggressive therapies, and second, identifying which patients are going to respond to treatment.

Now in this area I'll share you some emerging data on something called quantitative sensory testing, or QST, which is also being used in other painful conditions. UPMC and Johns Hopkins, in collaboration with the University of Aalborg in Denmark have done a series of evaluations on QST.

Our colleagues in Denmark have come up with a simplified protocol called pancreatic QST or P-QST, which is a series of evaluations that can be done in 15 to 20 minutes and can also be done in an outpatient setting. We use something called temporal summation, pressure detection or tolerance in different areas of the body, and condition pain modulation.

And based on the response from the patient we can stratify a patient into one of three groups-- patients who have normal pain processing, patients who have something called segmental sensitization, that means sensitization in the teeth and dermotrim which is the peripheral representation of the pancreas, and patients who have central sensitization, or sensitization even in other areas of the body, with the hypothesis that these patients are the ones who may not respond to therapy as well.

Now looking at a cohort of about 180 patients, we found that about 50% of patients had normal pain processing and that the remaining 50 had either segmental or widespread sensitization. The figure on the right is very illustrative because in the extreme right column, patients who had painless chronic pancreatitis, the large majority of these patients have normal pain processing.

On the other hand, patients who had painful CP at the time of evaluation had higher prevalence of segmental or widespread sensitization, suggesting that there is modification of pain perception in these patients. These preliminary data along with the pilot study demonstrating that patients with widespread sensitizations have a lower response to treatment has been the basis for now an ongoing clinical trial at Johns Hopkins and UPMC to determine whether QST can predict outcome in these patients.

Because of a number of knowledge gaps in chronic pancreatitis and how diabetes and pancreatic cancer relate to this, the two institutes of NIH, the NIDDK and NCI established a consortium called CPDPC in 2015. This consists of 10 clinical centers and a data coordinating center.

One of the studies of the CPDPC is a longitudinal observational study in adult patients with chronic pancreatitis called PROCEED Study. What you see here is The PROCEED cohort, or the representation of the distribution of the PROCEED cohort, where individuals are organized all the way from patients who have no pancreatic disease-- or who are normal volunteers-- all the way to patients who have definite chronic pancreatitis.

The sample size had been chosen to address epidemiologic outcomes in these patients, as well as using the biorepository that is being developed to identify diagnostic and prognostic markers of the disease. A cohort is now assembled, about 95%, and we are starting to analyze some of the data and I'll share some of that with you in the next few minutes.

In one of the first evaluations we assessed for quality of life in these patients and presents a behavioral and psychological comorbidities. So similar to the NAPS2 data that I showed you in around 500 patients, about 25% patients reported mild to moderate pain, and about 69% reported severe pain. Patients who had severe pain had higher prevalence of constant pain with 2/3 of them reporting constant pain.

In contrast, patients who had mild to moderate pain, most of these patients had intermittent pain. We use the PROMIS 29 and PROMIS Global Health questionnaires to assess quality of life. What you see here is a PROMIS 29 profile of the seven different domains.

And a simplified way to represent the data is that quality of life in patients with CP with no pain was very similar to patients who had mild to moderate or intermittent pain. It is the presence of severe pain or constant pain that resulted in significant decrement in quality of life of patients.

The other way that we evaluated this data was using the response to the questions we were able to generate t-scores to categorize patients into whether they will qualify for a diagnosis of moderate to severe symptoms of anxiety, depression, sleep disturbance, or low physical function.

The prevalence of these psychological and behavioral comorbidities in patients with CP as compared to controls was very high. But among patients with CP, it was patients who have severe or constant pain where the prevalence of these were three to five-fold greater as compared to patients with no pain.

The question here comes up is, is this a cause and effect phenomena? But more important questions is if you address prevalent, psychologic, and behavioral comorbidities in these patients, would that improve pain management? And this was address by an ancillary study of the consortium that was led by Dr. Tonya Palermo at the University of Washington.

In this study, which was published last year, the first aim was to refine an existing internet-based Cognitive Behavioral Therapy, or CBT, self-management program to chronic pancreatitis. Second was to conduct a pilot randomized clinical trial for feasibility and acceptability. And third aim was to generate preliminary data for outcomes of interest.

The study was done at four consortium centers and the National Pancreas Foundation also helped to advertise the study on the social media outlets for recruitment. What was shown is that the CBT program was highly feasible and recruitment was feasible.

Over 50% of patients who were approached for the study participated, the retention rate was very high, and engagement with the intervention, as well as completion of the telephone modules was very high. The acceptability was rated as 80%, and there were a lot of positive qualitative reviews we received from patients.

In terms of outcomes of interest, a composite outcome of either pain indifference or pain intensity at three months in patients who had CBT as compared to waitlist control was significantly higher. We also noted trends in improvement in quality of life.

These data suggest that evaluation and management of psychological morbidities and behavioral comorbidities in these patients can help to improve pain management. These preliminary data have formed a basis for a more definitive trial that is currently under review.

So coming back to the pain management algorithm, we do follow a multidisciplinary approach in our practice where gastroenterologists, surgeons, nutritionists, and pain management specialists evaluate and make treatment decisions. What is lacking systematically in the field is assessment of psychological and behavioral comorbidities and addressing them to see if that would improve outcome.

The second thing that I touched upon was utility of new evaluation strategies that could help to predict outcome for our treatment in these patients, like the QST.

Moving on to another set of results from the PROCEED Study is a high prevalence of osteopathy that we noted in patients with chronic pancreatitis. So in over 500 patients with definite chronic pancreatitis, we had 282 patients who underwent a DEXA scan to assess for bone health.

And what we found is that a very high fraction of patients had either osteoporosis or osteopenia. So if you look at men, where we typically don't think about osteopathy, 40% have either osteoporosis or osteopenia. When you look at more hard outcomes, the prevalence of traumatic fractures or spontaneous fractures in patients with definite chronic pancreatitis were significally greater than patients who did not have osteopathy.

Another way to look at the data is with increasing age, especially in women, we do consider osteopathy as a possibility, but we do not consider this in patients who are less than 50 years of age. And if you take that criteria, then about 30% to 35% of patients with CP had osteopathy which you will miss if you would not do a DEXA scan.

When we looked at the factors that are associated with development of osteopathy, we found that traditional risk factors dominated. For example, increasing age, female, sex, white race, and being underweight. What is missing is chronic pancreatitis related factors were not associated with osteopathy.

This, in part, is related to maybe a small sample size, say for malnutrition or exocrine insufficiency, but other factor is that it may be a result of more systemic effects of chronic inflammation, which has been documented in other GI disorders like inflammatory bowel disease or cirrhosis. In these conditions, performance of DEXA scan on a regular basis has been included in guidelines. For chronic pancreatitis newer guidelines are starting to incorporate that.

Another aspect that I want to cover is pancreatic enzyme replacement therapy in patients with chronic pancreatitis. More recently, we used a nationally representative health insurance claim data called PharMetrics that has over 48 million enrollees. And over a 13-year period-- 2001 to 2013-- we identified all patients who received a diagnosis of chronic pancreatitis.

Our aim was to determine how often these patients are assessed for exocrine insufficiency, how often they are prescribed pancreatic enzyme replacement therapy, and how often is the dosing appropriate? What we found is that in less than 10% of patients testing for exocrine insufficiency, or in other words, a fecal elastase, fecal chymotrypsin, or quantitative fecal fat was performed.

Less than 1/3 of patients received a prescription for pancreatic enzymes, and less than 10% of patients who received a prescription had appropriate dosing. Suggest that there is a huge margin for improvement in terms of assessment and treatment for exocrine insufficiency in these patients, which has a potential for improving nutritional status in patients with chronic pancreatitis.

The standard recommendation for pancreatic enzyme replacement in these patients is about 50 to 70,000 units, lipase units, per meal, and half of that with snacks.

So to summarize chronic pancreatitis section-- response to currently available therapies for pain in chronic pancreatitis are suboptimal. QST is a promising tool to predict which CP patients with pain are more likely to respond to invasive therapies.

Chronic pancreatitis patients have a high prevalence of psychologic comorbidities and evaluation and addressing them may improve clinical outcomes for pain management in these patients. CP pain patients have a high prevalence of osteopathy, and a DEXA scan should be considered in these patients for assessment. And oral pancreatic enzyme replacement therapy is often underutilized and under dosed.

With that, I thank you for your attention. And during the chat during my presentation, I will be responding to your questions in the chat. Thank you so much.