

SPEAKER: Thank you all for joining us. It's really a pleasure to co-host this with my good friend and colleague, Chuck Conway. And today we will be talking about the multi-disciplinary management of pancreatic fluid collections, specifically inflammatory collections.

And we're going to run through some of the data, and really more about how we approach these together with the combined surgical and interventional GI approach. I think before we even start-- Chuck, I'm sure you agree. But I've found that a lot of people use various nomenclature for these.

So I think it's important that we all think about what we're talking about, and are we all speaking the same language with this. I'm going to use the terms that have been put forth as the revised Atlanta classification in 2012. And we'll refer to this as-- an acute peripancreatic fluid collection is a peripancreatic fluid within four weeks of an episode of interstitial edematous pancreatitis.

Some of those can go on to pancreatic pseudocysts. We'll talk about that. We'll refer on a-- sort of on another side are the acute necrotic collections. And those are collections with variable amounts of fluid, and necrosis that involves the pancreas or peripancreatic tissue. And these occur after an episode of necrotizing pancreatitis.

Some of these over time can go on to being walled-off necroses. I just want to make sure that we all kind of use the same terms as we think about this. What do these look like? These are a series of images from a recent publication by Peter Banks in *Gut*. And at the top left is an example of an acute peripancreatic fluid collection.

So this patient had acute interstitial pancreatitis, and had some fluid develop around the pancreas parenchyma. Over time some of those can develop into what's on the lower left, which is the pseudocysts. This is more walled off, but what's inside is all fluid.

On the top right is an acute necrotic collection. That actually has variable amounts of fluid, as well as solid tissue, which has necrosed. But it's not yet well-encapsulated. Some of those over time can develop into walled-off necrosis.

Now as we approach this subject I think it's important to recognize how much of a problem is this. Well, about 300,000 ED visits and about 200,000 hospitalizations were documented in the US in 2002 related to acute pancreatitis. About 80% to 90% of those represent interstitial edematous pancreatitis. And 10% to 20% are necrotizing pancreatitis.

Amongst patients with interstitial edematous pancreatitis, greater than 90% will resolve. But some will develop into pancreatic pseudocysts. Among acute necrotic collections over four weeks time those can progress on to walled-off pancreatic necrosis.

Who needs treatment for these? Well, treatment is really based on having symptoms. Infection or suspected infection's probably the number one cause of somebody being considered for treatment of a pancreatic fluid collection. This can occur in about 20% of patients with necrotizing pancreatitis.

Keep in mind that there is a time we used to think about FNA-ing these to assess whether they're infected or not. But routine FNA is really no longer indicated. Because clinical signs accurately predict whether somebody is-- whether we ought to be concerned about infection in greater than 90%.

Other indications include ongoing organ failure. About 40% of those actually will have infected pancreatic fluid collections. And then less common indications for treatment would include having a mass effect resulting in outlet obstruction, having refractory pain or weight loss, bleeding into the pancreatic fluid collection. I don't know how often you've seen that, Chuck. But it's considered a rare event.

CHUCK Yup.

CONWAY:

SPEAKER: And probably even rarer, things like abdominal compartment syndrome or bowel ischemia. But I think we've actually shared a couple of patients, even, with concern for the lowest one there-- bowel ischemia.

Now when we think about treating these patients, I think it's important to recognize that delaying treatment actually will improve outcome. There was a randomized controlled trial in the late-- in 1997 where they actually randomized to early versus late necrosectomy in severe necrotizing pancreatitis. And they found a significantly higher mortality rate in those undergoing early surgical necrosectomy. So that study was actually stopped early.

There was another more recent follow-up study performed in the Netherlands. This was one of the Dutch pancreatitis cooperative studies. And this was actually a very nice interesting study. They actually looked at mortality based on time to intervention in 242 patients in their cohort.

And they found that the longer one delayed to doing any kind of intervention. That could be surgical, percutaneous, or endoscopic. But that longer time to intervention was associated with a lower mortality rate. So again, I think this sort of supports the general consensus, even when we talk, of trying to delay treatment when possible.

Now in terms of pseudocysts-- symptomatic pseudocysts that require treatment-- how best should we approach these? Well, I think surgical cystgastrostomy or cystenterostomy has been considered the gold standard. Other options obviously include percutaneous drainage, endoscopic cystgastrostomy, and EUS-guided gastrostomy.

How do these compare? Well, the studies on surgical versus percutaneous drainage or symptomatic pseudocysts, most of these studies are from the 1990s. Surgery in these studies was more definitive than percutaneous treatment. However, there was a higher mortality with primary surgical therapy. And usually, percutaneous therapy was really used as a bridge to surgery.

Endoscopic versus percutaneous drainage for symptomatic pseudocysts has been compared to similar technical and clinical success rates and adverse events. However, there seems to be a higher re-intervention rate, and a longer hospital stay with percutaneous, favoring the endoscopic side.

Standard endoscopy to EUS-guided drainage has been compared. There have been a couple of randomized controlled trials. Both suggest higher technical success with EUS, essentially because in some of these patients on standard endoscopy that bulge that's needed to target the pseudocysts can be difficult to identify. There were no differences in adverse events, although the rate was higher in the endoscopic drainage.

And lastly, again specifically for symptomatic pseudocysts, EUS has been compared to surgery. There was a randomized trial from Alabama where they compared 20 versus 20 patients-- EUS versus surgical. There's no difference in treatment, success, complications, or re-interventions.

However, there was a shorter hospital stay, lower costs, and a better patient well-being in the EUS arm. So all of this really supports more on that endoscopic, or probably specifically, EUS-guided side.

When we kind of approach this for our patients, we essentially stick to what's recommended by international pancreas guidelines of a conservative management first, followed by drainage, followed by a surgical or endoscopic debridement if needed. I will say that has been the case, although I think lately we've started changing our algorithm maybe a little bit. Maybe we can discuss that a little bit more when we look at some of our cases.

CHUCK OK.

CONWAY:

SPEAKER: When we talk a little bit more about the data, too, I think it's important that we focus on three trials, which I think are actually quite important. These are three randomized controlled trials related to necrotizing pancreatitis that needed intervention. All came from a multi-center Dutch co-operative pancreatitis study group.

One was the PANTER trial, which patients were randomized to step-up, drain, and then debride, versus primary open necrosectomy. A second trial was the PENGUIN trial, where endoscopic necrosectomy was compared to surgical necrosectomy. And the last and most recent was the TENSION trial, in which patients were randomized to an endoscopic step-up approach, versus a surgical step-up approach, which involved video-assisted retroperitoneal debridement and open if needed.

So the PANTER trial was the first of these randomized trials. This was comparing step-up approach or open necrosectomy for necrotizing pancreatitis. They randomized 88 patients.

And in the step-up group alone it's important to know that drainage alone was sufficient to treat patients in 35%, meaning that they put in the drain, and they would have gone to the next step if needed. But 35% of the patients actually did well with drainage alone. That was sufficient therapy.

They looked at their major complications, which they described as multi-organ failure, multiple systemic complications, perforation of a visceral organ or major bleeding, and death. And they used a composite score of this. And they found that the rate-- that the odds ratio to have major complications was higher in the open group compared to the step-up approach.

So based on that trial, that sort of reinforced this idea of drainage first, followed by debridement, and that delay to getting that if needed. The second trial from that same study group was a trial comparing endoscopic transgastric necrosectomy versus surgical necrosectomy. And all of these patients were for infected necrotizing pancreatitis.

They randomized 10 patients in each arm. And in the surgical arm they started with the video-assisted retroperitoneal and proceeded to open it. VARD was not possible. Amongst the endo group it was a median of three procedures. Two patients actually ended up also getting treated with VARD via a percutaneous drainage tract. And 40% actually had prior percutaneous drainage.

In the surgical group they had six VARD procedures, and four underwent laparotomy. And interestingly, 80% actually of those patients also had prior percutaneous drainage. They looked at a variety of outcomes, notably a pro-inflammatory marker, IL-6-- that was lower. As well as the reduced major complications/death index was lower in the endoscopic versus surgical group. And based on that, they favored that this endoscopic approach to necrosectomy was probably favored over the standard surgical techniques.

The last trial they did was actually the TENSION trial. In this they actually randomized to a step-up approach endoscopically versus a surgical step-up approach, using similar techniques that were used in their prior trials.

This is actually the results that they presented at last year's European gastro week. And they found that the primary endpoint of major complication or death was similar in both arms. The percent not meeting necrosectomy after initial drainage was similar in both arms.

However, they had a higher rate of pancreatic fistulas than the surgical step-up arm, and they had a longer length of stay in the surgical step-up arm. Obviously, this also translated to lower costs in the endo group. So their data actually, for those reasons, favored the endoscopic step-up.

Now I think what's actually quite interesting is the concept of endoscopic necrosectomy. Can it be performed earlier or not? This was actually a very interesting study from the Brigham group published in 2014, where they, over a period of time actually, offered patients the sign that they needed some sort of procedure for their walled-off necrosis.

They actually went straight to direct endoscopic necrosectomy. And they matched that cohort of 12 to a prior cohort where they did the usual step-up approach, where patients who developed symptoms got a drainage. And then followed by debridement surgically if needed.

So they found-- their main outcomes they found was that the length of stay was shorter when they went straight to direct endoscopic necrosectomy. And health care costs were five times more in the step-up group, favoring that maybe with these techniques we can get access to that necrotic cavity transgastrically. That maybe we're doing patients-- maybe we're doing better for patients by going quicker to direct endoscopic debridement, rather than waiting for that step-up. I just thought that was a very interesting trial.

Now the concerns with endoscopic debridement of walled-off necrosis. There's many concerns. I mean, they sort of emanate from how the technique works. What we often used to do was get access into the cavity, put in a couple plastic stents to keep it drained.

And then when debridement was needed go back, pull those out, access that tract again, dilate it, and then go into that cavity and perform direct endoscopic debridement. This required a large tract diameter-- a large tract dilation, with the risk-- an inherent risk of perforation, bleeding, or leak.

It required multiple intubations into and out of that cavity, which can be kind of tricky when we don't have access into that, and it can be difficult to visualize. And then it required maintaining that tract for subsequent procedures, because often this wasn't done at one session. In systematic reviews and meta analysis on this, complications range in the 20% to 35% range using that traditional endoscopic debridement technique for walled-off necrosis.

What I found very interesting is this new advent of-- or a new approach to this using these lumen-apposing stents. This allows us to really create a nice port into that cavity to access and take away many of those negative features of the more traditional way to do endoscopic debridement.

Some studies on this, which I was fortunate to be part of-- this was actually the first clinical experience in which mainly pseudocysts were drained. There was a couple other drainage procedures done overseas. And in this-- using this technology, 15 pseudocysts were successfully treated.

A follow-up to the study I wanted to share that I was also fortunate to be part of-- this was from a multi-center effort for EUS-guided drainage of peripancreatic fluid collections and necroses, using these newer lumen-apposing stents. We looked at a series of cases.

There was 14 pseudocysts, 68 walled-off necroses. Technical success was actually higher with the walled-off necrosis in this study. But we think probably because most of the pseudocysts were performed earlier, and there were some initial stent maldeployments based on operator error. With more experience it beared towards a much higher success rate.

The number of endoscopic sessions needed obviously varied, based on whether it was a pseudocyst or walled-off necroses. But the long-term success was very high for both groups, both pseudocysts and walled-off necroses.

I'll end sort of some of our didactic slides with kind of sharing what Chuck Conway and I do when we approach these patients together at our center. We still try to think about those traditional principles of, you know, in the acute setting delay any treatment if needed.

In the non-acute, so greater than four weeks out, and somebody needs treatment, for pseudocysts it's mainly we think about a drainage procedure. And for symptomatic walled-off necroses we start thinking about debridement procedures.

And what we do is we actually discuss these together in a multi-disciplinary format, often at a case conference. Occasionally we actually piggyback even these sort of benign cases into our upper GI tract and hepatopancreatic or biliary tumor board conference, just because all the relevant parties involved are usually present.

Again, we'll initially err towards a conservative management, supportive care. But when treatment is needed, and if it's less than four weeks-- which means the wall is immature-- that's where we really think about whether percutaneous drains or immediate surgery is the best approach.

If treatment is needed but the wall is a little bit more mature there, then for pseudocysts we actually favor endoscopic therapy over percutaneous IR drainage. And by that we're talking about usually an EUS-guided cystgastrostomy. And for walled-off necroses we actually have a real thorough discussion about is this a candidate for direct endoscopic necrosectomy. And we'll share with you some cases where we think patients were candidates for that.

And if not we start thinking about whether percutaneous drains need to be placed either in route usually to surgery, depending on that clinical situation. What I would like to do, I think-- and what we both want to do is kind of share a couple of cases that-- well, probably more than a couple of cases that we've shared over the last year and a half or so that we've been together in our center.

Case one is an 18-year-old male with a history of necrotizing pancreatitis. That was about four months ago. He now came in as an outpatient-- I saw him in the office. And he had complained of nausea, vomiting, and early satiety. We'll play this video.

There it starts. So this was the initial CT four months prior, and that shows an acute necrotic collection. And then clearly at that point we both agree there's not much to do, and he didn't really need anything for it. Four months later this was much more walled off.

And Chuck Conway and I discussed this together, but because of its close proximity to the stomach we went ahead with an endoscopic procedure. So on this we put a cautery-tip lumen-apposing stent. You can see that under EUS-guidance going in. That's the inner flange. This is the luminal flange. You could see fluid draining directly.

Now, I often-- this was an outpatient, actually. And if there's no other concerns, I'm not overly concerned about underlying infection, I'll often go in right away doing that index procedure. So I dilated the stent. This is a 15-millimeter version.

And I often usually take it up to about 13.5 just to make sure that I've got a nice opening, but yet I don't push the stent in or out. And kinda work on it with snare devices. And I do what I can at that first session.

And usually we'll work on it, time permitting, of 10 hours or so getting what we can. And then I'm still a fan of putting some dilute hydrogen peroxide. And this patient actually went home. And then we'll often bring them back at a few-week intervals to do additional.

I know this is somewhat debated whether one needs to, or just leave it and bring them back for a final procedure. But I just feel like I'm able to see it and get things-- get some of this material out. I don't think we're there yet knowing what's the best approach.

So I've been a fan bringing these patients back, and remove more necrotic tissue. In the interim I usually take them off PPIs. I want stomach acid to get in there and help break things down. I actually also put them on a TID of a carbonated beverage, thinking that it might help break some of that down.

CHUCK Sure.

CONWAY:

SPEAKER: So this was the cavity on the fourth procedure. There's still a little bit of debris whether you take it out. So a couple of weeks later on the fifth we just removed it, and the cavity looked pretty healthy. And that's sort of the gastric defect after removal.

I'll go on to one other case before we-- I think we have some other cases where necessarily the endoscopic method wasn't always the best approach. But the second case is a 29-year-old male. Actually, Chuck and I shared this case about-- I think six weeks ago. Something like that.

Paraplegic male. He had a history of severe necrotizing pancreatitis, was treated at an outside center with a percutaneous drain eight weeks prior to him coming to us. Then about two weeks prior to him come to our hospital that drain had been dislodged and was removed.

And I think Chuck actually came down to your service, I believe, when the outside surgeon had called you. And he was having fevers, elevated white cell count not looking great, and transferred I think to our center for discussion of surgical debridement. And we can play this video.

But this was that initial CT in our hospital. And you can see there's a few air pockets in that walled-off cavity. So we actually-- this is one of the ones where Chuck called me in on the Sunday to do it. We go in when needed, and this was needed.

So at that initial placement I actually just placed the stent. We had pus draining out. And in subsequent endoscopies while he was an inpatient, we took out large bits of necrotic tissue. I think you saw some of those there.

And this was actually treated as an in-patient, because he was pretty sick. I think he was growing out gram-negatives in his bloodstream, too. And as an inpatient we brought him down every few days to do it. And finally, I think he had some placement issues, so he was with us for a few weeks. But we actually were able to remove this during his hospitalization as well, and clear him of all that necrosis.

I think now we have also some other cases.

**CHUCK
CONWAY:**

Yeah. I was going to end-- thanks, Janic. And thanks everyone for joining us. I'm going to talk about a couple of cases. I think that the cases that Janic has shown, and the data he's shown, I think makes it pretty clear that endoscopic therapy definitely plays a role. And really, it's becoming more and more kind of the primary treatment option, really.

There's a few places where I think surgery still plays a role. And we'll sort of talk about that in a little bit. But certainly, I do think most of these cases, just like our cancer cases, should be talked about in a multidisciplinary kind of setting. So that you can sort of decide what's best for the patient.

I also want to point out the first couple of cases I have were totally non-operative. This is a 63-year-old gentleman that had biliary pancreatitis. And I initially saw him-- and we saw that the CT scan on the top there. And really, I sort of talked to him about how this was going to be quite a while, like they needed debridement down the road.

But ultimately, he just actually got better. And they ended up taking out his gallbladder later on. Really, he's done quite well. So I think giving it time and sort of letting things evolve is extremely important.

And this is another case, too. This was a post-ERCP pancreatitis. You can see on the left CT scan the fluid collection.

SPEAKER:

Wasn't one of mine.

**CHUCK
CONWAY:**

Yeah, right. It actually wasn't. That's true. But fluid and even air in the collection. And really, she was doing fine. She was able to tolerate diet, maintain her weight. So we just sort of gave her some time, and clinically she was doing OK. And we sort of let it evolve. And ultimately, we just needed a drain in a relatively small kind of inferior right collection.

So I think it's important also to remember a lot of times, just like from that PANTER trial, all of those patients don't-- a lot of patients will not need more than just a small drainage.

This is a case that I did do an operative necrosectomy on. You can see there's a large collection with necrotic debris and air, sort of extending laterally next to the spleen. And this is a sort of pretty typical story, where the patient sort of gets through the acute phase, and then just kind of has a failure to thrive, and loses weight. Just doesn't ever get the energy back. And you do a CT scan and you see this.

So we did a retroperitoneal drainage, where we asked the interventional radiologist to put a drain in through the left flank, which is sort of shown in the top picture there. And then we took the patient to the operating room. And it's really quite a simple procedure just to cut down on that drain. You don't need any sort of image guidance. You just follow that tract. And you can get in there and do the debridement.

Here's the picture from the radiologist. They went a little more posterior just because of where the spleen was. We like to have them go on the flank as much as possible, so that when the patient's sitting or laying down it doesn't hurt. But ultimately, got into the cavity for us.

And then the left is just a still but the right is a video we can play. And you can see I've got my blue gloves on there, using a ring forcep to pull out this necrotic debris. And you can see the incision is pretty small, sort of about probably an 8 to 10-centimeter incision. And someone just puts a retractor to pull to the side the abdominal wall musculature. And with sort of some careful kind of tugging, you can really get a pretty good purchase on the large amount of necrotic debris, and clean up the cavity pretty fast.

SPEAKER: How long do you wait before doing this after the percutaneous drainage?

CHUCK CONWAY: Oh. You can go the next day. I mean, it's just really a guide. And then you literally just cut right on the drain. So you're able to get the necrosis cleaned out quickly. Generally just one procedure. I do leave a drain and we can irrigate if we want to.

The downside, of course, is the pancreatic fistula that you talked about. Most-- probably at least a third of these patients, especially one that collection is up towards the pancreas itself, there's probably still communication. And you'll end up with a fistula. So you really can get large chunks pretty quickly, though, and get it cleaned out.

This was another patient that we did. This collection, you can see is sort of quite right lateral along the lateral wall, the duodenum. Again, had a drain placed here. And this is an area that I think sometimes you have a little more trouble sort of clearing out endoscopically. Put the IR drain in and then, again, did a small cut down on it.

And then this particular patient is one that I've done a esophagectomy on, and he developed post-esophagectomy pancreatitis. And you can see ultimately did develop some walled-off necrosis. So he didn't really have the anatomy that would be appropriate to put an AXIOS stent in or something like that. So again, we did this sort of minimally invasive approach where we got the guidance, and then cleaned that area out.

So I think as far as surgical interventions, I think certainly failed endoscopic management, which is becoming less and less. Lateral collections that are difficult to reach endoscopically. If there is some sort of anatomic reason it's difficult to get to. But it's important to remember a lot of times you are going to end up with a pancreatic fistula.