BroadcastMed | bsc_final_bridge-to-surgery-presentation-by-dr--muthusamy-mid.mp4

DR. MUTHUSAMY: Hello. My name is Raman Muthusamy. I'm the Director of Interventional Endoscopy and on the faculty at the University of California Los Angeles. It's my pleasure to discuss biliary metal stent bridge to surgery.

We have really made a lot of progress with regards to our ability to detect pancreas cancer, and I think before we can talk about staging and management of pancreas cancer, we really should talk about what is our algorithm for tumor detection. So initially if you suspect tumor, the initial step is usually to do a noninvasive CT or MRI, usually with find called pancreatic protocol, which instead of the standard 5 millimeter cuts are usually 2.5 millimeter cuts, or in some cases even 1 millimeter cuts. And at that point either a mass will be identified and then staging will be performed with the cross-sectional imaging, usually you get a CT.

But if no mass is seen, really the next step in the algorithm should be to proceed to an endoscopic ultrasound, which is really the most sensitive test for detecting small pancreatic lesions, particularly those under 2 centimeters.

This is an example of a case that I had at UC San Francisco many years ago. This is probably about 2002, when EUS was still sort of coming into its own even at major academic centers, let alone in a more community setting.

So this was a patient who was ultimately referred to me. Initially he had had some abdominal pain. There were some concern whether he might have some form of a malignant process. So he originally had a CT and an MRI, both of which were negative. And for unclear reasons he actually also got an ERCP, which was also negative.

And then ultimately at that time I was relatively new. They decided to give this newfangled EUS a shot and see if there would be potentially some value in doing an EUS. And lo and behold, there was a small lesion that you can see on the top picture. It was about 13 by 13 millimeters.

Now, normally this lesion looks like it's entirely confined to the pancreas. One could argue that it doesn't need a biopsy; it could simply be resected. But I knew at that time, with all the negative studies that had been done before, that I would probably need a tissue diagnosis. So I performed an FNA, which confirmed adenocarcinoma of the pancreas. And then I contacted surgeon who was quite surprised, given all the negative previous workup. And he subsequently proceeded to repeat each of the tests individually a second time. So the patient ultimately ended up with two CTs, two MRIs, two ERCPs, all of which were negative.

And he then came back to me and said, "Well, you know, I think I want you to take a look at that again and rebiopsy it." And I told him that I under no circumstances would do that since I was confident in what I had seen, unless he was willing to come into the room and watch it directly with me.

So at that point he said, "OK, I'll take the patient to the operating room," and was kind enough to send me this photo, which showed exactly what I had shown him, the 13 by 13 millimeter lesion that was in the pancreas. And this was an R-zero resection, and this patient's done well and continues to send me Christmas cards even now, even though I have left San Francisco many years ago, and he's doing very well.

We started doing a lot more EUS after this at UCSF, so it shows you the power of a case,. But again, really the detection of EUS is really quite superior to any other modality we have, especially for small lesions in the pancreas. So always consider doing an EUS in these situations if there's clinical suspicion but negative imaging.

So once you've made a diagnosis, what are the main questions after detection of pancreas cancer? Really the questions are, does the mass appear surgically resectable? The goal, of course, is to try to give patients who are potentially curable the appropriate therapy, but we really want to avoid unnecessary in patients who are not going to benefit from surgery. There's nothing worse than opening and only closing to find that the patient was staged incorrectly and isn't resectable.

And so the goals are to determine what is the predicted TNM stage. And we are increasingly moving to neoadjuvant therapy for locally advanced tumors, or even in some cases borderline tumors and in patients with regional lymph node involvement, with the goal of downstaging these patients.

So in preoperative staging, really there's four major categories. There's patients who have very localized disease, no extension to any of the arteries, to celiac, to common hepatic or to superior mesenteric artery. They have a patent superior mesenteric vein and portal vein confluence and usually a fairly small lesion confined to the pancreas, maybe obstructing the duct. And usually if there is nodal disease, it's usually quite localized.

On the other end of the spectrum, which we see, unfortunately, far more common than resectables, are the patients with metastatic disease. These are people who have either distant disease; it's either in the chest, mediastinal lymph nodes, which are present in 3% to 5%, carcinomatosis, disease in the lungs or liver, or may have disease in lymph nodes that are far from the primary lesion. So for head of pancreas lesions, the celiac artery, and as I mentioned, mediastinal adenopathy.

Most patients, however, are going to fall somewhere in the middle, which is either borderline or locally advanced disease. In borderline disease you've got a tumor that's in the pancreas that is abutting the superior mesenteric artery, but involves it for less than half its circumference. And it's usually a patient who's got unilateral, again, less than half involvement of the circumference of the superior mesenteric vein or portal vein or in the region of the confluence.

Now locally advanced disease is basically somebody who's got celiac, superior mesenteric artery encasement, which is defined as greater than 180-degree involvement. These are usually ultimately staged as stage III because of their significant T4 involvement, with more than 180-degree involvement of the vessels.

So here's a picture of a patient who has a resectable cancer I saw many years ago at the VA at UCSF. The patient presented with weight loss and jaundice. And you can see here a pancreatic mass involving the duodenal wall here. As you can see, the mass is hypoechoic, crosses into the duodenum. It's 3 centimeters in size and because it involves the duodenal wall, it's stage T3, but it doesn't involve any vessels. And this is a patient who has what we would feel would be resectable pancreas cancer.

In contrast, here's a patient with unresectable cancer who has presented again with weight loss and pain, has a 4-centimeter hypoechoic mass that you can see here in the center and the body, tail of the pancreas. And you can see here the superior mesenteric artery involvement. You can see the SMA takeoff from the aorta and you see the black mass and the SMA essentially are touching. And you don't see a white line separating as you do on the right side, kind of right at the 6 o'clock position in the mass, suggesting a loss of fat plane and direct extension into the artery. So this is a T4 lesion, not amenable to immediate resection.

This is a patient with borderline resectable disease, also not entirely resectable at the current time. And what you see here is that you see a hypoechoic mass. You see the SMV and the SMA, actually, but they both have essentially a fat plane that's present, especially the SMA, throughout. The SMV has a fat plane in some areas, but in small areas the fat plane is sort of lost. So this is less than 180-degree involvement, and this would be an EUS borderline resectable disease for that reason.

So what do you do with the staging? The lucky few who are resectable can go directly to surgery. Patients who are metastatic, of course, are typically treated with palliation. But patients in the middle, which is the majority, either have locally advanced disease or borderline resectable, increasingly are moving towards a strategy in which they undergo downstaging chemotherapy, usually for three months but for sometimes longer. And these patients are then subsequently attempted to be made resectable with treatment.

For patients with head lesions, they're going to require an ERCP with stent to relieve any malignant obstruction. And we have better chemotherapy these days than we did in the past. So we actually can downstage patients. In the past, it was kind of viewed that chemotherapy was really palliative and only slowed the march. It was a little bit like the old days in HIV and CD4 counts. Once you hit a certain number you'd never go back above that number. It was only a one way elevator.

Well, we now have much better regimens, and with better drugs and longer therapies and the right combinations we're actually able to achieve some significant regression of tumors, to the point where many of these patients can be made resectable.

The indications for tissue diagnosis in suspected pancreatic cancer-- again, you're trying to get a goal of obtaining a tissue diagnosis in a variety of situations. Obviously if you've got metastatic disease and you need a diagnosis to start treatment, you need a tissue diagnosis for that. If you've got a patient who is high risk for surgery and you want to make sure that when you operate on him that you're dealing with cancer and not something else that maybe isn't cancer or just inflammatory, you may want a biopsy in that patient. And patients, again, where there's not clearly a lesion, maybe a lesion. You want to really confirm that there's something there, maybe, before operating.

And then sometimes there may be that you see a mass there and it looks clearly resectable, but you're not sure it's the kind of mass that needs resection or could be treated medically. For example, if you have a lymphoma of the pancreatic head as opposed to an adenocarcinoma. Obviously, lymphoma would be treated nonoperatively.

But tissue biopsy is indicated when it will affect the treatment plan. However, it's not indicated when it won't impact the treatment plan. So if you've got a young, healthy patient who's got classic symptoms-- weight loss, jaundice, and a mass on CT that appears resectable-- you know, if the patient's got a positive biopsy they're going to go to surgery. But if it's negative, you're probably still going to assume it's tumor and it's also probably going to go to surgery. And so ultimately it's not clear what the value of the needle is because you're going to do the same thing either way.

And I would argue that the patient I showed you from UCSF years ago with the 13 by 13 millimeter lesion was probably someone who actually didn't need an FNA. But at that time, I knew that my surgeon would not be inclined to take that patient to the operating room without a clear tissue diagnosis, given the number of previous negative studies.

The major paradigm shift that's occurred with the management of pancreas cancer has been that in the past, people who had borderline disease or maybe even somebody who might even have a scan that suggests that they have locally advanced disease, they didn't want to ask too many questions, because the real attitude was their best chance for cure was with surgery. And surgeons obviously had a self interest in this. But they really, I think, were taught to believe that this was true. And this is where a lot of people thought this was true.

So in general, you tried to get every single person you possibly could to the operating room. You didn't ask a lot o questions. Many people didn't undergo extensive preoperative staging for fear that they might find something that might preclude them from surgery. And really, the feeling was the only chance you had was with surgery. It was certainly understood that surgery didn't cure everybody. In fact, it didn't cure most people. But it was really-- the only cures that did occur were from surgery, and so you at least wanted to put yourself into that pool.

And that concept at that time was try to cut it out if there was a positive margin. If there were some lymph nodes that were positive, you would treat that on the backside with adjuvant therapy. The problem is that there are surgical complications, sometimes patients have a hard time recovering, and that during this time the residual disease was going untreated. And there's disease progression. So patient age, their preoperative performance status, co-morbidities, and some patients even just simply refused after how bad they felt after their surgery.

In fact, about a third of patients did not receive adjuvant therapy in a trial that was done at MD Anderson. And this is not unique to MD Anderson. So if you take a look at other institutions, the Mayo Clinic, Hopkins, the national data from Medicare, the SEER database, all found that only about half of patients typically receive the intended adjuvant therapy. In fact, MD Anderson was above the curve; 2/3 of their patients got therapy, which is actually higher than all these other groups.

So the goal of treating on the back side doesn't happen about half the time. So you operate, maybe you leave a positive margin. They never getting anything else because they had issues with surgery and really aren't up for it, and ultimately the disease goes unchecked and the ultimate outcome is poor.

Because so few patients receive adjuvant therapy, the results have been relatively poor with this strategy. So if you take a look going back to mid '80s, actually there was an initial study just comparing 5-FU and radiation of adjuvant therapy to surgery alone, you did see about a nine-month benefit. But several other studies that have looked at this have found a four-month, couple of four month benefits, a three-month benefit, another four-month benefit.

And so what you're getting for doing this is not a huge amount of time. You're really getting probably somewhere in the range of three to four months in most of the larger and more recent studies. And that really leads to the fact that we need a better algorithm to treat this disease. We've tried it this way for 25 years. Our numbers are not great. We know that the majority of these patients are dead within five years. We are not really achieving a lot of progress in this. And really the goal of trying to get people to surgery and treating them in the back half, as I've just shown you, hasn't really borne out the results that we really need.

The advantages of treating upfront is that it treats the real problem in pancreas cancer, which is micrometastatic disease. How many times have patients gone for an operation, had a victorious R0 resection with negative margins, only to show up at their first follow up visit with a scan showing three new liver lesions? And the reason is those lesions were probably all there; they were just not seen at the time of surgery because they were too small to be really detected. And the advantage of a neoadjuvant approach is it treats not only the known disease, but it also treats unknown disease. And it provides treatment of micrometastatic disease, which is present in probably 80% to 90% of patients, who are "resectable."

Patients with rapidly progressive disease, will we avoid subjecting to surgery with this? Because if you've got someone who's sort of borderline resectable, you start giving him chemo and then six weeks later they've got five liver lesions, that's a person that if you would have taken him to the operating room, they'd have done the same thing. It's not like you would have done any better. And you probably help avoid the morbidity of the surgery for that patient.

It's a good local strategy for the incidence of positive margins. You know, a lot of times people will try to tackle these big lesions because they feel surgery is the only option. They leave some tumor behind. Maybe the neoadjuvant approach would make these a little bit easier to manage.

Delayed recovery is also not an issue because you're getting treated upfront before you get the surgery. So you're going to get the treatment. You're not going to be part of this 35% to 50% of people that never receive the treatment because you're too sick postoperatively. So these are all advantages with this sort of approach

Micrometastatic disease, again, is widespread. This is a study that was published in 2011 where they took 48 patients who had had an R0 resection. Basically they felt that the margins were all clear. They had gotten all of the primary tumor. And then they went and looked at the lymph nodes that they had harvested from here.

Now, there were 31 patients in whom they harvested lymph nodes, even though they had gotten a negative margin and what they felt was all the primary tumor. 31 out of the 48, so basically somewhere in the range of 2/3, already had lymph node mets. OK? So there was disease outside the pancreas. But of those patients, essentially the remaining patients almost virtually all had micrometastatic disease when they ran special markers looking at even the nodes that were negative, they were positive too. So essentially everybody had node-positive disease, suggesting that even the patients who you think you have it all, you usually don't, either at a macro- or microscopic level.

And this is the reason I think that the surgery first approach, without taking care of the micrometastatic disease has yielded us little benefit over the years. We've taken a different approach at UCLA, and again locally advanced pancreas cancer prolonged preoperative treatment is associated with lymph node negativity and excellent overall survival. So at UCLA it's not uncommon not only to not get just three months, but either six or nine months in terms of therapy.

And this is a study published by my colleague at UCLA, Tim Donahue, looking at a retrospective review of almost 20 years, 1992 to 2011, all patients with locally advanced or borderline resectable pancreatic ductal adenocarcinoma who were treated and received downstaging chemotherapy, with chemotherapy and/or radiation. They looked at the patients who successfully had surgical resection with biopsy or surgical pathology confirmed PD, pancreatic ductal adenocarcinoma.

So 50 patients who previously had been deemed unresectable ultimately were able to go to surgery using this approach. Again, what you see here is a CT of a patient who initially had quite a large tumor on the left. And the red circle shows that there is vascular involvement. And then this patient, after receiving neoadjuvant therapy, had a marked reduction, you can see, in the size of the tumor. You can see the vessel is now patent, CA 19:9 dropped, the functional status was good. And you can really see that there's a marked reduction here, as the new circle on the right shows, in the primary tumor.

So if you look at the baseline patient characteristics, patients on average were 60 years old. It was about 2/3 female. Most of the lesions were in the head. There was vascular involvement in all patients. In three patients they were unable to determine exactly where the vascular involvement was. It wasn't recorded in detail, as this was a retrospective study. The vast majority had portal vein and SMV involvement. About a quarter had SMA involvement, as was the same with the hepatic artery. And the celiac artery and IVC involvement were less common.

And if you take a look at the median followup, it was almost a little over four years. You see that a little over half the patients had no recurrence at the last followup. Local recurrence, which I think is the most striking finding, was only 12.5%. So you took all these people who had originally locally advanced disease, or borderline resectable, and when you look at these patients years out, they don't recur locally. So I mean, you're able to back this off, you're able to shrink this, and you're able to cut it out and keep the margins essentially negative over a long period of time.

Distal recurrence, which again, from micrometastatic disease and so forth is a bigger problem, which is 54%. And then unknown was about 33%. And really the disease free for survival, people went for about two years doing fine without any known disease, and their overall survival was really almost 3 and 1/2 years. And most striking, the five-year survival, which has been our surrogate term for cure, shows that about 43% of patients were able to make it five years. Which for a patient who initially was locally advanced or borderline resectable is really, I think, amazing data. It gives us some hope in this disease.

So considerations in the neoadjuvant approach. You're going to require more often to get tissue prior to treatment. You're going to need durable biliary decompression. It's going to be required particularly for patients, obviously, with head lesions and biliary obstruction.

And it's going to require physicians to work together to coordinate care. The endoscopist is going to-- it's not just you diagnose the cancer, they go to surgery and then they become post-op patient. Now you're going to be involved in maybe even pain control in some of these people with celiac blocks. You're going to do tissue diagnosis. You're going to stent them when needed. And really it's going to require close collaboration between you, your surgeon your oncologist and maybe your rad oncologist.

So what are the challenges to this changing paradigm of switching from surgery first to surgery in appropriately downstaged patients who have had a good dose of neoadjuvant or downstaging chemotherapy? I think there's probably four major issues. One is are SEMS better than plastic? The second is if I choose a SEMS, should I choose a covered or uncovered? Number three, you're telling me that it's better to expend a stent at least probably 20 times more expensive than a standard plastic stent? How are we going to justify this in the theory of cost containment? And number four is how's this going to affect the chemotherapy and the delivery of the chemotherapy.

So this is a study showing plastic-- metal stents for malignant common bile duct obstruction. You see the median patency here, plastics 57, metal 126. Total time in hospital is less for metal stents. The median survival was about a month and a half longer for metal stents. So this was not particularly significant in this study. And again, I don't think there's a huge amount of debate that metal stents are going to give you better patency than plastic stents. They're obviously much larger.

Here's another study of 113 stents placed in 52 patients. 70 were plastic and 43 metal. Some of the plastics were ultimately converted to metal. And you can see, this Kaplan-Meier sort of failure shows that the metal stents, with the time of survival of the stent, you can see that on three instances in a year, about half of the metal stents are still active, whereas you see under the plastic stents, about half are still active in only about 90 days. So you can see that this is really a marked difference in terms of durability.

We looked at the issue of plastic stents in patients undergoing neoadjuvant or downstaging therapy for obstructive pancreatic cancer that was causing jaundice and biliary obstruction. So we looked at four centers, 1996 to 2013 434 patients, of which we had ultimately 173 we had full data on. This of all 233 stents that were placed.

The median patency we found for stents in this situation, even though it's supposed to be 12 weeks or 84 days, was only 53 days. And some patients had their stents removed at the time of surgery. But if you looked at those who sort of continued on to an ERCP exchange, this group had an overall stent patency of 61 days. And again, that was in a large number of patients, more than half of this group, that didn't end up getting their stents pulled in surgery. Had to come in early, due to either worsening LFTs, which you can see 41 patients had, or cholangitis. And these patients, again, a pretty short duration of stent patency, 40 days and 56 days.

So really these patients require more frequent stent exchanges. Here's the data again presented in a graphical form. At three weeks you can see 80% of all stents are patent, but already by six weeks you see barely over half are patent. By nine weeks less than half, and by 12 weeks only about one in four to one in three stents is going to make it that long, even though that's what the manufacturer recommendation for the durability of this is.

This is another slide just basically showing the same data, 233 stents. Median stent patency was 53 days in about half of-- there was a large number of these that ended up with stent-related admissions. Again, some were related to the surgery, surgery group. This is the routine exchange group. And the premature exchange group, of which, again, about half were from worsening LFTs and most of the rest was due to cholangitis.

And if you just look at the group that had routine versus premature exchanges, again you see the median patency was just a little over eight weeks, so pretty poor.

Moving on to challenges, we've shown that plastic stents have reduced patency in this situation and that metal stents are probably superior to plastic. The question is which mental stent? Should I use covered or uncovered?

So this is a randomized controlled trial that was done using self-expandable metal stents with the anti-migration system. These are partially covered stents, and they were compared with uncovered stents for distal biliary obstruction caused by pancreas cancer. And this was a randomized trial in Japan.

And you can see here the main take home is that the covered stents, which is the red, is above, doing better. On average, it looks like about it gave you an extra 55 days in terms of time without any kind of dysfunction or problem. So you've basically got six months versus four months. You've got about two extra months with basically worry-free problems with issues of the stent.

Now if you take a look at overall stent patency, so now this means that you could-- maybe you've got some sludge or some food that's causing distal obstruction-- you go in, you sweep all of it out, and the stent still works. So you can do some interventions, but as long as you don't have to place a new stent, the stent was considered patent. So if you use that, then the covered stents are really good. They don't have much in the way of tumor ingrowth, and a little bit of cleaning here and there of sludge allows you to get a median patency of really a remarkable over a year and a half, compared to probably somewhere in the range of around 10 months with an uncovered stent.

So this is really some pretty encouraging data that we see here. Looking at this randomized trial again, you see stent dysfunction in about 22% of the uncovered group-- I'm sorry, 22 patients in the uncovered group, which is 37%. Which trended toward more than in the covered stent group. And again, the main difference is uncovered stents have a large number of patients, 25%, who end up with tumor ingrowth. And this just doesn't occur with the covered stent. You may get a little bit of overgrowth and some sludge formation, but you don't get this. And this was statistically significantly less tumor ingrowth in patients with covered versus uncovered stents.

So other challenges that you're going to encounter, the issue of is it cost effective. So you're telling me you want me to try to place a more expensive stent in this era of cost containment? We did a study looking at this to see which strategy is less expensive. We compared plastic stents initially in patients undergoing downstaging chemotherapy. We chose an elective exchange every 10 weeks. This was done before we finished our other study, where we showed it really should only be about seven weeks.

Oh, we talked about placing an initial metal stent with replacement of the stent in case of an occlusion. Patients with borderline resectable pancreas cancer were the ones that we chose to involve, and we chose downstaging chemotherapy and again, biliary obstruction would be required for patients with head lesions and requiring endoscopic decompression.

The outcomes we looked at were what were the likelihood of death, surgery, or tumor progression over the course of this treatment. We looked at the outcomes of stent placement with regards to migration, occlusion and cholangitis and factored those in. We looked at Medicare costs for procedures and hospitalizations and manufacturer costs for stents.

We used a decision tree using the TreeAge software program comparing, again, placement of a plastic stent initially with elective exchange every 10 weeks, or a metal stent initially with replacement in the event of occlusion p.r.n., and then calculated estimated durations based on the literature.

And the endpoints were making it to one year; making it to successful downstaging-- we modeled what percent of patients typically would be downstaged; what was the likelihood if you develop tumor progression, so that you are now getting worse and you are no longer really in true downstaging mode, for more palliative mode; or death.

And we looked at one year cost strategy, and we ran two-way sensitivity analysis to see what it would take for one strategy or another to completely dominate the other. And this is the model that we chose, and this is just to give you a schematic of the tree we created utilizing all these different scenarios in our TreeAge program.

And our base case estimates showing what were the ranges. So we assumed in base case, plastic stents would occlude within the 10-week period about 15% of the time, and then we came up with a range that was reported in literature. The rate of migration for plastic to be 5%, the rate of occlusion for SEMS to be 15%, migration for SEMS to be 2%, and so forth.

You see that initially ERCP cost is a little over $2000 because it's a little bit more than what you get for the replacement exchange stent, because getting access can be a problem. And Medicare knows this, and so they give you more for the initial access and less for the subsequent stent change. Plastic stents are cheap. We know that. $83. Metal stents were modeled at about $1,000, and there's the price you see at $4,255 for hospitalization related to pancreatitis or another complication.

So we see the one year treatment cost strategy is about $6,571 for a SEMS versus $17,000 for a plastic stent. So it's about a third as expensive to start with the SEMS. And this is because you save ERCPs by having longer duration of patency.

So when we looked at the threshold analysis, we found that plastic stents would only be viable if you could make the stents last at least six months, which is 190 days. I've shown you that they barely last six weeks. And then the ERCP cost has to be dropping to less than $380, which, while costs have dropped, they haven't, and hopefully won't ever get to that level.

With regards to SEMS, the duration of stenting period needs to be as long as it's more than 136 days, and increasingly we're moving to longer and longer neoadjuvant treatments and the cost of the metal stent is under $12,000, which is, again, our price is only about $1,000. Then it wins out, which shows why there's such a huge advantage in favor of SEMS.

And the final challenge I will discuss is maintaining patency during chemotherapy. In this case, we're talking about the role of these two stents with regard to patients who are actively receiving chemotherapy. Metal stents definitely reduce the risk of chemotherapy postponement due to stent occlusion, because this occurs more frequently in plastic stents. The bilirubin goes up, you have to stop therapy, the tumor potentially has a chance to go unchecked.

And you see the complications are seven times higher among patients with plastic stents than metal stents. And there's a three times higher rate of hospitalization in patients in the plastic stent group, leading to delays in care, more costs, and a potential for tumor to grow unchecked during these periods.

Most oncologists I've spoken to are happy with a bilirubin under 2. Some will treat up to 4, but most people are very uncomfortable treating with bilirubin of more than 4, because some of the oncology drugs are actually excreted through the biliary tree, and if that's obstructed, patients can develop toxicity from these drugs accumulating.

So in summary, SEMS are better than plastic. Covereds are better than uncovered. Cost effectiveness is favoring SEMS because of the reduction in the need for ERCPs and hospitalizations. There's an advantage for chemotherapy for SEMS due to the reduction in the number of times therapy may be delayed.

Do you always need a mental stent? No, not always. I mean, obviously if the patient looks like they have very resectable disease, you may not need to stent them at all. You may be able to go directly to surgery or you may be able to put a plastic in the short term, for just a couple of weeks before the patient gets their surgery, but may not need any neoadjuvant therapy.

Some general themes and trends in treating pancreas cancer. Again, increasingly nearly all patients are going to receive preoperative downstaging chemotherapy. This is done to treat micrometastatic disease that's not always visible currently on any available modality. The use of this neoadjuvant therapy is going to require pretreatment EUS-FNA for tissue diagnosis. You're going to see more and more EUS done to make a diagnosis.

Given the fact that many of these patients are going to require more than three months of treatment, durable biliary stenting is needed. And the fact is that many patients receiving downstaging therapy are still going to fail and are going to eventually progress and never become operative candidates. And they also will benefit from really durable stenting.

Plastic stents, we know, have reduced patency in the setting of neoadjuvant therapy, probably on average about a little over seven weeks. The use of short covered metal biliary stents is preferred, given their prolonged patency, because they're much wider diameter. Their covering allows preventing tumor ingrowth. And short stents avoid complications of surgical resection by avoiding the hilum and also reducing the chance of covering the cystic duct in patients with intact gallbladders.

Now remember, even if you do cover the cystic duct and a patient starts developing signs of cholecystitis, you can always pull the stent. It's a covered stent. And just change it out for a plastic. So don't necessarily need to go to surgery.

The reported rates of cholecystitis and stent migration with fully covered stents are very low, single digits. Stent migration can predict tumor response in some cases, and may even decide that you don't need a biliary stent any more, because your tumor has shrunk enough, you're not getting obstruction. Patients with suspected cholecystitis can easily have their stent removed as well.

So in closing, the NCCN has national clinic practice guidelines of the National Comprehensive Cancer Network, and they write these guidelines for many diseases, including pancreas cancer. And the pancreas cancer just underwent a revision for 2014. And this group is really comprised of all kinds of stakeholders. And there's people who are surgeons who treat this disease, gastroenterologists, radiation oncologists, medical oncologists, internal medicine doctors, interventional radiology, pathology, patient advocates.

So they really get together, look at all the available evidence and make recommendations. And based on the information in part that I've shown you today, they've revised their guidelines. So you see for 2014, for anybody who's undergoing borderline resectable patient with no metastases and was getting planned neoadjuvant therapy, they recommend placement of a stent, preferably a short metal stent, if biliary ductal obstruction is present. And again, that's based on some of the data that we've just shown you and others.

Same thing for locally advanced unresectable. Even if you don't have a cancer diagnosis confirmed, they say that you're probably going to need to get that confirmed, and if you're jaundiced, go ahead and place a short mental stent. And if it is confirmed and you're planning downstaging therapy, again, you do an expandable metal stent in that setting as well.

So the paradigm has really changed. We've really gone from an operate first, ask questions later to really trying to treat everybody, try to treat that micrometastatic disease. Avoid having these early recurrences because there was disease present outside of the pancreas at the time of surgery. And really select for the patients who are most likely going to get benefit. And with that, I think we can hopefully achieve a real meaningful change in the way we get results in treating pancreas cancer and hopefully we'll see some positive results finally in managing this disease. I thank you for your attention and for listening to this lecture.