BroadcastMed | Cytoreduction (CRS) with Hyperthermic Intraperitoneal Chemotherapy (HIPEC): Specific Clinical Situations

Konstantinos Votanopolous, MD: Thank you very much for being here. I would like to give you the inside story of how we truly select patients at the Wake Forest University. So, the reason we are here today and discussing about the topic is because there is a major change in the concept we see peritoneal disease. In other words, what's happening is that back in time peritoneal disease was a synonym of a stage lV {} disease. Well, it seems like for a group of patients for whom we don't know why, and we don't know how, it behaves more like a locoregional problem. And this is why you will hear us discussing and writing about the term peritoneal surface disease instead of peritoneal carcinomatosis. So, I will be very brief with this stuff because we've already discussed about them. The goal of the operation is always complete macroscopic cytoreduction. And we take the patient to the operating room and usually place stents. We open the Pandora's box and then we place four cannulas at the cytoreduction: two below the diaphragm, and two in the pelvis. You can see the outflow cannulas. We perfuse the patient for two hours with heated chemotherapy, and then we close-- we wash the aisle to close and he's going to ICU for a day. But, the whole process is how do we really select these patients. It is imperative for the patient not to have disease outside the peritoneal cavity. It would be the extreme exception to operate on a patient with disease outside the peritoneal cavity. This does not have retroperitoneal involvement. Chemotherapy does not penetrate more than three millimeters of tissue into the retroperitoneal. The functional status should be very good and nutritional status should be excellent. Favorable tumor biology and liver disease is should be easily [? resectable. ?] This is not the time to perform an anatomical resection. So, in other words, you have your biliary obstruction, and you have your ureteral obstruction. You could have a small bowel obstruction more than one side or micro level obstruction. You get have disease of the gastro- hepatic ligament, or you could have more than three parenchymal liver lesions. And if the PCI is more than 20, then your chances to achieve known optimal cytoreduction has to run high. Now the PCI score is nothing more about the what the doctor [INAUDIBLE] introduced like 20 years ago, 50 years ago. You divide the abdomen into thirteen areas and you give a score depending on the size of the solid lesions. Keep that in mind because all of that are good, but what we're trying to avoid is we are trying to avoid to opening the patient and get into something like that. This is a disease. That is not the bulk of it because the small bowel is essentially loaded with tumors. And this is a similar situation here. This is a situation where cytoreduction is not possible. This one though, is totally different. This is a guy who has a metal caging but this is not a deal breaker because, as you can see underneath, there's more bowel that is spared. By the way, whoever is seeing this picture and keeps questioning what is the role of laparoscopy, in the [INAUDIBLE] diagnosis, you can do a laparoscopy. But with these types of [? for ?] [? metal ?] caging you have to think two things. One is you cannot move your metal cage. This is going to be lateralized adheres to the lateral peritoneal wall. The other thing is you could try to do a biopsy. You have to be sure that all of this [? lops ?] [? bopseum ?] on the peritoneum, it's not more bowel incorporating into the disaster. So that's fine. This is a rough guideline of how we select patients. But they don't really apply to everything. They don't really apply when you have a patient with ascites, when you have obese patients, elderly, or eventually patients who will come back with a recurrent disease. And this is an example of why they don't apply. How are we going to calculate the PCI score on this patient when you cannot see the solid component of the disease? The only scene you see here is a lot of fluid with a gastric bulb, and the spine. So is this a candidate for an operation or not? So, we know very well that when you have ascites, the chances to receive a complete cytoreduction is only 15% When you don't have ascites, you can achieve a complete cytoreduction up to 60 percent. So who is the 15% that you will end up taking to the operating room? So we went back to the peritoneal surface disease database we have and we found about approximately 310 patients with ascites. While there was a variety of cases, the majority of them were appendiceal cancers. And then we created something that we call an ascites score. And the ascites score is nothing more than we take the patient when he is on the CAT scan table, the fluid will go to the most dependent part of the body. We divide the abdomen into nine areas that are identical to the areas that you use to calculate a PCI score. Each one of these areas is assigned with one point even if it's fluid, and to give a score between zero and nine. And after that, we went in and we calculated the ascites score of the CAT scans. And we've seen-- we noticed that a patient with an ascites score between one and three-- that means up to three areas of fluid in the peritoneal gravity-- has a chance to achieve a complete cytoreduction of 38%. But when the score goes down to four or six, it goes down to 10. And when it goes down to 7 or 9, the chances to receive a complete cytoreduction is only 7%. So, in other words, to achieve a complete cytoreduction on a patient with an ascites score of seven is like asking yourself, do I really feel lucky? And why this is important, this is important because this is the difference in median survival between a patient who can have a complete cytoreduction, with ascites, and the patient who has an incomplete cytoreduction with ascites. One is living for 5.6 months and the other one is 37 months. So, in other words, if you take a patient with ascites, for anything else besides a low grade apendiceal cancer, if you take him to the operating room, to give him a procedure with 5% mortality, 40% morbidity, and to drop the quality of life between three and six months for him to live six months, you don't really help him. So what we are saying is ascites score is an important tool for patient selection. You know that ascites is indicative that you will not be able to achieve complete cytoreduction so select them appropriately in order to avoid a trip to the operating room that doesn't help anybody. Now, the next category of patients is the obese patients and the question was OK, I have a morbidly obese patient-- 39% of this population is obese-- and obesity does not really spare peritoneal carcinomatosis. So, is the morbidity of the person an acceptable high end for this population? So, we went again back to the database, we found 246 patients and 40% of them had severe obesity with a BMI of more than 35, as classified by WHO criteria. Their morbidity and mortality were identical. Actually, the mortality was less in the obese than the mortality in the non-obese. And the only difference-- and this is a busy slide-- but the only difference between the groups was the difference in their admission rate. There was a late admission rate of one to three months for the obese patients, mainly attributed to intra-abdominal abcesses and infection. The pattern of the complication was also identical. 26 different complications were identical between the groups. What was also different-- interesting though, was the survival. Between the colon cancer patients, there was no difference in survival between obese and non-obese. I think this is because they don't live that long. As you can see, the impact of obesity into their long term outcomes. But for patients who have low-grade appendiceal primaries, they will live for a long period of time. There was a difference for patients who had a BMI more that 35. So severely obese patients live less than the remaining. And when we went back to see why do they really die, the interesting thing was that they didn't die because of cancer. They died because of other comorbidities. There was a trend between 14 to 28% that there was not statistically significant due to other power, but there was a trend toward death from comorbidities. Now, the most difficult group of patients to decipher, at least for me, is the elderly population. And, when I'm talking about elderly, a I'm talking about patients who are more than 70 years old. This is because, when we review the experience from 1992 to 2013, the 30 day mortality for this population is 13.6% versus 3.9 for patients who are less than 70, and the 90 day mortality was 27.4%. So with these numbers, you start wondering should I be doing these operations on this population? And, then you go down to the survival, and you see the survival for a gastric cancer patient, who is elderly, is only 7.6 months. So we say no, not for gastric cancer, with the possible exception for a positive cytology, a positive {} or a PCI that is less than six. Colon cancer, you have to be really careful because they don't do as well. But for appendix, mesothelioma, or ovarian, they live something between three and five years. So, who is this patient that will do well with a high age range? In the univariate analysis, as you expect, the year of the procedure was significant because it reflects the institutional experience. It reflects the fact that back in time, when Wake Forest started doing operations that were not selection criteria, because we didn't know who was the appropriate patient to be operated or not. But over time that was developed, and this is why you will see the drop in mortality. The complication was significant and additional stuff which was also significant, and as you expect, the primary site of origin is also significant. Now, in the multivariate analysis though, what is significant in predicting survival in the elderly is the type of primary, the albumin, and the completeness of the cytoreduction. But when you take in this model, and you include the complications in the multivariate analysis, the only thing that remains essential for these patients to survive is the institutional experience, and the absence of the complication. And these plots illustrate all of the above. You see that after 2004 there was a significant drop in the morbidity and mortality. 2004 is the mid-level of our experience, volume-wise. On the second plot, you see that patients who really do well are the appendiceal, mesothelioma, and ovarian cancer, where gastric and colon cancer are not doing that great. But what is really important is that in this group of patients, if they get a complication, they lose every survival benefit. The median survival for these patients with the complication is 13 months, without the complications is 39 months. So they

don't delay the HIPEC. If you operate on them, everything should go perfectly well. And the question, of course, is what predicts a complication in the elderly? I've listed our experience. The volume of disease predicts a complication, so the more organs you take out, the more complications you will have. Every gram of albumen decreases their complication by 40% so you need to have a real normal albumen level. Comorbidities doubles their risk of a complication. And for the smokers, and the difference was between 38 and 8%. Now eventually all of these patients with a recurrence-- not all, but I mean, the majority will come back with a recurrence. And then the question is, should they be doing a repeat cytoreduction in this population? Is the morbidity and mortality acceptable? So only 7.7% of the database were able to have a second cytoreduction. The median follow up for this group was 60.8 months. The median ICU and hospital stay were identical. To 30 day mortality and morbidity was exactly the same, 3.2% and 48%. A CCR [INAUDIBLE] was achieved in 43% and the median survival after the second cytoreduction was 52 months for appendiceal cancer, 21 months for mesothelioma, 53 for ovarian, and 55 for colon cancer. And if you achieve a complete cytoreduction, the survival is twice the survival you have without a complete cytoreduction. On multivariate analysis, what was really important in predicting survival for repeat HIPECs is the completion of the cytoreduction, and the interval between the first and second operation. In other words, it's everything about selection of the patients and by loss of behavior. Because if it's a longer interval, the less they are to have a systemic failure. And in conclusion, ascites is a strong predictor in the ability to obtain being a complete cytoreduction, a strong predictor. Mobility is not a contraindication. You have to be very careful with patients that are more than 70 years of age. Any complication in this age group depletes any survival advantage. And for complete cytoreduction, if you are able to do it, you can reset the clock. And with that I would conclude, and I will answer your questions. Thank you.