Discussion of 2021-1780

SURVIVAL AND ROBOTIC APPROACH FOR PANCREATICODUODENECTOMY: A PROPENSITY SCORE-MATCH STUDY

**DR MANNY ZERVOS** (Greenville, NC): Dr Rosemurgy and his colleagues have once again reported the superiority of the robotic approach to pancreaticoduodenectomy in terms of blood loss and hospital length of stay, non‑inferiority in terms of complication, readmission, and mortality rate, and inferiority with respect to operative duration when compared with patients undergoing open pancreaticoduodenectomy in their high‑volume program. These findings are supported and well established in multiple studies looking at not only the robotic approach for pancreaticoduodenectomy but also other surgical procedures.

The novel finding, and 800‑pound Neanderthal in this room, is the stark disparity in the median survival that favors the robotic approach, 41 vs 17 months, an almost 2‑and‑a‑half fold improvement in survival, with anecdotal application of neoadjuvant therapy and only a roughly 50% chance of receiving any chemotherapy at all.

Previously, such dramatic improvement in survival for this disease has been attributed to addition to or modification of established multimodal chemotherapy regimens, as in the recently published PRODIGE 24 trial, which reported a median survival as high as 54 months in patients undergoing resection and perioperative chemotherapy. Dr Rosemurgy readily admits in his manuscript that the survival advantage associated with robotic pancreaticoduodenectomy is inexplicable, offering cytokine modulation as a possible explanation.

But before I trade my double‑posted OMNI for the da Vinci Xi so that my patients can also live longer, I have the following questions:

Why did you use only age, sex, and American Joint Committee on Cancer (AJCC) stage in your propensity score rubric? Would the analysis change if you captured more of the global experience by including other factors like optimal pancreatic surgery, postoperative pancreatic fistula, or early postoperative death?

Compared with other published data, your median survival for patients undergoing robotic pancreatectomy is higher than expected, and lower than expected in the open group, especially for the matched cohort. Do you have any insight as to why this is the case, and why propensity scoring in and of itself shortened median survival by almost 7 months?

How will you follow up on these data? During our years together, when unexpected findings occurred, you would say, "You don't make the news; you just report it." But a survival advantage of this magnitude demands either a prospective randomized trial or at least some explanation, not only to convince skeptics but also accelerate transition to the robotic platform beyond the early adopters, such as yourself, which I honestly believe is the direction we are heading.

Dr Pitt reported a steady increase in neoadjuvant therapy from 13 to 48% between 2012 and 2020 for patients undergoing pancreaticoduodenectomy. The tide you and I are swimming against is increasingly strong. Under what circumstances would you consider neoadjuvant therapy in resectable pancreatic cancer?

**DR HENRY A PITT** (Philadelphia, PA): The observations with respect to increased operative time, decreased blood loss, and shortened length of stay are not new. However, the author's claim that robotic pancreaticoduodenectomy leads to increased survival compared with open surgery is unique. The major question is whether this conclusion is justified.

First, 30‑day mortality among the 521 patients was 8%, as I calculate from the manuscript, which is 3 times the national NSQIP mortality rate. Also, 90‑day mortality was approximately 16%, which is about 5 times the current national data. The serious morbidity rate was typical, which means that the failure to rescue rate was very high.

In the paper's discussion, the authors comment on the importance of anesthesia, critical care, and interventional radiology colleagues to support rescue of patients who have developed complications. Thus, my first question is, how can you have a high‑volume pancreatic surgery program without building a multidisciplinary team to rescue your patients?

Second, the manuscript does not state the time frame which was reported. Presumably, more open operations were performed earlier in the analysis, while most of the robotic procedures were done more recently. Importantly, the manuscript does document that the 75 matched open patients had higher 90‑day mortality and were significantly more likely to receive a gemcitabine as adjuvant therapy. In comparison, the 75 matched robotic patients had lower 90‑day mortality and were significantly more likely to receive FOLFIRINOX postoperatively, which is a more effective chemotherapy regimen. Thus, in my opinion, the reported survival difference was due more to the postoperative mortality differences and the less effective adjuvant therapy in the open patients and was not the result of the operative approach. Please address the short‑term mortality and adjuvant therapy differences as the potential real drivers of the reported difference in survival.

Third, I have some concerns about the propensity score matching methodology. You matched only one‑third of the 210 open cases and one‑quarter of the 311 robotic patients. Thus, the numbers in both groups were relatively small compared with the overall experience. What was the match tolerance, 0.20, and were the patients matched for a study year? Again, why were they not matched for 90‑day mortality and adjuvant therapy? Ideally, a match tolerance of 0.02 with more patients as well as matching for 90‑day mortality and adjuvant therapy should be performed before any claims can be made regarding survival.

**DR MARYBETH HUGHES** (Norfolk, VA): Did you discuss the percentage of patients who underwent adjuvant chemotherapy, and did they get to chemotherapy quicker if they had a robotic operation? This would be intuitive but may not be correct and may explain your differences.

The decrease in estimated blood loss may change your transfusion in those patient populations. We know that transfusions are a negative predictor of good outcome. Please clarify those two things.

**DR BRYAN CLARY** (San Diego, CA): I suspect you also apply a robotic platform to your distal pancreatectomies. I am curious as to whether your survival experience is similar in distal pancreatectomy adenocarcinoma.

We can apply technology not just in the operating room, but to our other processes. For example, regarding your comment about having a lack of awareness of patients who trickle through your emergency rooms in the post‑discharge setting, there are ways through your electronic health record to set up automatic notifications so that you know when your patients are anywhere within the hospital system. We have recently done that at the University of California, San Diego in a pilot study. I at least know when my people are in the emergency room in a somewhat real‑time fashion using Epic Chats.

**DR WILL CHAPMAN** (St Louis, MO): I saw the Clavien‑Dindo III or greater complications, but I did not hear the actual fistula rate. Can you tell us what that was for both groups and how that was defined?

**DR ALEXANDER S ROSEMURGY, III** (Tampa, FL): Our hospital is an interesting place. I wrote a paper after having been there for a couple of years: "Where the Pancreaticoduodenectomies and Pancreatic Surgeries and Liver Surgeries Are Done Is Not as Important as Who Does Them." I must backtrack on that. For context, I have probably been through 8 or 9 interventional radiologists. They are so busy putting in central lines and ports that if I want an angiogram done on a patient, I must perform a CT angiogram first to document that there is, in fact, an issue. If it is 11:00 at night, God help us, because they may be at another hospital putting in ports and lines.

The ICU doctors are medical doctors, and they see ventilators hooked to patients. They do not see patients who are in the ICU on ventilators, for example. It is a different perspective.

We do not have a strong working relationship with the anesthesia team. I often do not know the anesthesiologists performing the procedure on the patient, and often I do not know any of the attending anesthesiologists who may go through that room during an operation, and I do not know the certified registered nurse anesthetists because they rotate. The hospital gets a contract, then a new contract. They get different groups. It is a constant revolving door.

I have concluded that this hospital, which used to be a sleepy community hospital, really wants to be a sleepy community hospital, and there is only so much change that we, as physicians, can make, particularly at this date and time when we are being commoditized by hospitals.

With that in mind, why the propensity score matching was performed with age, sex, and AJCC stage, I do not know. I do note that when we looked at it backwards, if we had stratified them by R0 resection rate instead, we could not have done better. The groups, I think, are very comparable, and any differences we see should be due to the issue here.

I do admit that mortality is very high. It is what it is, but it must improve going forward. The patients did not die of a single problem, they died of a very small incidence of many problems.

Why is survival better with the robotic pancreatic approach? I do not know the answer to that question. I have looked at several proinflammatory cytokines, TNF, \* IL‑2, I have run the gamut of them, probably 30 different ones, and they are not different. I do not know why the patients do better, and I have been challenged to sort this out.

Regarding the use of neoadjuvant therapy, I would love to argue this with anyone who would argue with me. I do not buy into the entire concept of neoadjuvant therapy. Who would I treat it with? I would treat someone with locally advanced unresectable disease. I would give somebody neoadjuvant therapy if there was a comorbidity that needed treatment. They come in and have an A1c of 13. They need weight loss and diabetic management, so we will give them neoadjuvant therapy while we improve their medical condition, or they get catheterized and stented, or whatever the case might be, whatever the comorbidity might be, but I am a surgery-first guy, and I would love to do a prospective randomized controlled trial, or participate in one, if anybody is interested. I have written one.

Neoadjuvant therapy and adjuvant therapy were not protocol driven. In the manuscript, I note that I can document about 60% of the patients received adjuvant therapy, but I would not operate on a patient if they were not going to take adjuvant therapy. I would not do it. Those numbers just cannot be, but so many of our patients are cared for by medical oncologists far away, and we have an inability to properly follow those patients. Furthermore, I cannot protocol drive this because it would require so many principal investigators. It is unworkable.

I will say there are a lot of people over 70 years of age, who are genetically profiled not to respond to gemcitabine, and you know what they get? You got it, gemcitabine. I have several patients on capecitabine and 5FU and so on and so forth. It runs the real gamut.