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Discussion

DR. EDWARD M. COPELAND III (Gainesville, Florida): At the University of Florida, our group has used preoperative radiation therapy for the past 14 years, and Dr. Kirby Bland presented the results of this treatment before the Southern Surgical Association in 1991. Like Seigler's group, we compared our results to a nonrandomized control group with similar preoperative staging. Most patients were downstaged, and both survival and local control were significantly improved by preoperative radiation therapy.

We had fewer treatment complications in our patients, probably because we did not use concomitant chemotherapy. Currently, we are using continuous infusion of 5-fluorouracil in combination with preoperative radiation therapy, and our toxicity remains minimal.

Unlike Dr. Seigler's group, for some time now, we have tailored the operation to the status of the post-treatment lesion. If significant tumor regression occurs, we transanally excise the remaining lesion and ensure complete excision by frozen section control of the resected margins. For gross residual disease, an abdominoperineal resection, low anterior resection, or coloanal procedure has been done with satisfactory healing. I have several questions for Dr. Seigler:

I was surprised by your operative complication rate. The cisplatinum may be contributing to poor wound healing, is it necessary?

Now that you are beginning to tailor your operation to post-treatment staging, what are your criteria for transanal local excision?

Several control patients underwent postoperative chemoradiation. If you compare preoperative *versus* postoperative chemoradiation therapy, is there a benefit for giving the chemoradiation therapy preoperatively?

What has happened to the two patients who had a complete response and refused a surgical procedure?

Thank you for allowing me to discuss this paper.

DR. MARSHALL M. URIST (Birmingham, Alabama): Dr. Chari and Dr. Seigler are to be congratulated for this very clear summary of a group of patients that has been treated under very strict conditions so that we can compare them to other results. I enjoyed reading this manuscript very much and certainly enjoyed receiving it 1 month before the meeting. My questions are very similar to Dr. Copeland's:

First of all, why were the patients who were treated with this protocol chosen for this, and what were the differences in the other patient population? Specifically, were the operations the same?

How many surgeons are involved with the control patient population? I suspect that they were all treated by a single surgeon in the neoadjuvant treatment group. Were the procedures for the other patients as carefully done?

In regard to the control population, the patients in this group were treated according to the standard therapy of that particular time. The question is, did all those patients receive postoperative radiation therapy, and did they also receive chemotherapy?

Also, if they were treated postoperatively, then there was a specimen available. And how many of those specimens had positive lateral margins? Because we know that you really cannot compare positive lateral margin patients with those who had preoperative radiation therapy and then read something into the local recurrence rate.

Finally, these results are very impressive. You have seen statistically significant long-term survivals in these patients and significant decreases in local recurrence. Does this mean that this form of therapy is now the new standard of treatment? Do we now require a randomized trial? Where should we go from here?

DR. RAVI S. CHARI (Closing Discussion): Dr. McDonald, Members, I'd like to thank the discussants for their questions and their kind comments regarding the manuscript.

Dr. Copeland asked the first question about significant tumor regression and what type of operation should be performed. In our manuscript, we did allude to the fact that we are entertaining the thought of sphincter-preserving type of surgery. Right now, all these procedures were performed based on the initial pathology. The difficulty right now is that even though we saw 20 patients preoperatively by biopsy and sigmoidoscopy to have complete clinical response, only 11 of those 20, or 55%, actually had a sterile specimen. And that is a similar result to that reported from the Anderson trial, where they actually saw a lower number, only 36%, having actual sterile specimen. That segment which is going to be amenable to limited procedure still has to be determined.

His second question was regarding the role of cisplatinum. We are now changing our protocol to have continuous cisplatinum infusion to see if that decreases the complication rate. We feel that continuous infusion, such as he is using right now, may decrease some of the complications.

He asked if we did have patients—and this actually addresses one of the questions Dr. Urist asked as well—in our control group who have undergone some postoperative chemotherapy and x-ray therapy. To answer this question, we had 22 patients who underwent postoperative chemotherapy and radiation therapy in the patient population control group of 56 patients. These all came after 1990. Previous to that, we did not employ it on a routine basis. There were 21 T-3 patients and just one T-2, for a total of 22. We did not break that down, Dr. Copeland, to see if there was a difference in terms of preoperative therapy and postoperative therapy, but that is something that should be studied.

Dr. Copeland asked about the two patients who had complete response clinically and refused definitive surgery. As Dr. Seigler mentioned, we have seen those patients now 5 years out, and they do not have any complications or recurrence.

Dr. Urist's question regarding patient population and how they were selected: this is single-surgeon based for the protocol group.

And, finally, Dr. Urist's last question: is this the new standard? We closed our paper saying that the results in this paper should be interpreted with caution. There is a preliminary phase II trial, where controls were concurrent, but they were retrospective.

The exact role of preoperative chemoradiation now needs to be determined in a prospective randomized trial to determine whether preoperative chemoradiation therapy has any benefit over preoperative radiation alone, postoperative radiation and chemotherapy together or surgical therapy alone. I think this has to be performed prior to establishing this as the new standard.

Again, I'd like to thank the discussants, the Members and Dr. McDonald for the privilege of discussing this paper.

Thank you.