Discussion

Dr Todd L. Demmy (*Buffalo, NY*).

This article indicates that there is a preference in this scenario to offer the patients induction chemo, a macroscopically complete resection, no intraoperative adjuvant therapy, and then a selected postoperative adjuvant therapy, which for approximately half of the patients included radiation. Since your earlier publication in 2007, you increased your series from 18 patients to 72, and although you didn't mention it, my interpretation of that survival graph showed that you had no 30- or 90-day operative mortality, which is remarkable.

Your long-term survivals were worse with thymic carcinoma and R2 resections, which is expected, but many were prolonged series. And based on your own critique in your article, the benefit of surgery is somewhat uncertain because of the lack of a nonsurgical control group and the indolent nature of this disease that permits prolonged survival despite multiple unresected recurrences.

So because progression-free survival and our relative importance as surgeons in this disease may be determined by some tumor biologic marker yet to be determined, I would like to focus my 2 questions on your surgical decision-making in this setting, your secret sauce, if you will. The first relates to this Figure 1, which in the article you can view little slash marks, which tells if you have taken the patient back to surgery. When I looked over this, I noticed a couple of patterns. I saw that some patients had 3 to 4 repeat resections spaced every couple of years; they always received a resection; then there was another group who seemed to have 1 attempt at re-resection and then just watching recurrences; some had no attempts at resection; maybe a slight reduction in the number of re-resections from your first 18 patients to the next 18 patients.

How do you go about this. Is it a surgeon preference pattern? Can you give us some guidelines about these crucial decisions? Do you use histology? You didn't mention whether positron emission tomography imaging plays a role of this decision process.

Dr James Huang (*New York, NY*). Yes, I think so. In the figure, as you mentioned, you can see indications of where patients underwent re-resections for episodes of recurrence. Typically that would always happen, number one, if they were symptomatic for some reason; for example, there was a lesion that had spinal involvement or pain. That was one reason that they would go to surgery. So if they were symptomatic, then they would get treatment for that. In the absence of symptoms, I think that's where it gets gray,

and trying to distill that clinical decision process, I think generally if the disease appears like it's still potentially completely resectable in a patient with good risk, those patients would still be offered that opportunity. I think it gets a lot grayer when the disease is extensive and you don't know what the chances of getting a complete resection are, and the risk/benefit ratio becomes a lot more gray. Those decisions are sort of exactly what we are trying to get at with this paper in terms of laying out what really happens with these patients and setting expectations for them.

In terms of positron emission tomography, we generally don't use it frequently for these patients, especially those with thymoma. We use it more frequently for thymic carcinomas because of the more aggressive biology.

Dr Demmy. My last question relates to your surgical decision-making with respect to competing and emerging technologies. For instance, patients may find other centers that are offering intraoperative heated chemo or photodynamic therapy, and that being said, some early reports show that these thymic tumors have high programmed death-ligand 1 levels. Should a patient with stage 4b now be considered for referral to pembrolizumab or a similar immunotherapy trial?

Dr Huang. None of these patients received any intrapleural chemotherapy that was not done at our institution. I know several institutions have done that with varying results. I do think it does speak to some need for better some sort of adjuvant topical or local adjuvant therapy for these patients given their recurrence patterns. In terms of immunotherapy, there are immunotherapy trials ongoing for thymic carcinoma, but they generally have not been offered for patients with thymoma given the risk of autoimmune adverse events.

Dr Kenneth A. Kesler (*Indianapolis, Ind*). Would you say you are now less likely to surgically intervene in a patient with a small amount of pleural based disease, and, on the flip side, when you do surgically intervene, are you more likely to be aggressive with an EPP versus pleurectomy?

Dr Huang. If you see somebody and they show up a few years down the road and you see a single lesion, I think it's hard for us as surgeons to resist and say, oh, I'm just going to leave that alone when there is only a single lesion. So I think we are tempted, and we often will go in and take those out.

It is still debatable, and certainly this doesn't prove in any way that surgery is definitely impacting these patients. It is also hard, the reverse, to say to somebody who has known disease that is there, and even if it is slowly progressing, that they are just going to be okay with knowing that there is disease there when you potentially could take it out. I think that's a bit of a hard sell to some patients. But I think it is something that I actively talk about with them. I don't promise them that we are going to cure them when we take these patients back.

Dr Joseph B. Shrager (*Stanford, Calif*). So basically, at least in the thymoma subgroup, this is a local disease problem, or if you want to call thorough disease local disease. So I think the whole issue about some sort of local adjuvant is really critical. I'm sure Frank can tell us how far it has gotten,

but there has been talk for a couple of years of doing a prospective sort of a registry study using what Brian Burke has shown is quite active in thymoma cells, which is Betadine. And it seems like the first time you are there, because you don't really want to go back again doing an aggressive operation, maybe something simple like that, and we have actually started throwing Betadine into the chest in cases like this when they come along.