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ADULT

Discussion

Presenter: Dr Patrick M. McCarthy

Dr David H. Adams *(New York, NY)*. Thank you very much, Pat. I am delighted that I have the opportunity to discuss your paper.

I want to start the discussion by congratulating you and your team on these extraordinary results of mitral valve repair in patients with degenerative disease. These results are among the best reported and will influence future guidelines and help define what is possible in the contemporary era of surgical valve reconstruction.

Given the outcomes you now report, which asymptomatic patients with severe mitral regurgitation (MR) and preserved left ventricular function would you be willing to follow at this point? From 20,000 feet, it seems to me like the guidelines have it right. The presence of severe, degenerative MR should trigger treatment in the modern era if results approaching yours are achievable.

Dr Patrick M. McCarthy *(Chicago, Ill)*. Thanks, David. The decision is up to the patient. We're recommending surgery for typical patients. Sometimes they've just been diagnosed and it takes them a little while to become comfortable with the idea of heart surgery. They may want to follow with an exercise echo in 6 months. We may be more conservative if the patient has prolapse but no ruptured cords or flail leaflet. If they have only late systolic MR on echo, we also may suggest 6-month follow-up.

We use exercise echo often to help guide the decision. If their exercise capacity is good, and if the pulmonary artery pressures don't rise, then we're comfortable in watching them. But we counsel them to be carefully followed. We also educate them about the symptoms that they can develop and to return sooner. There have been sequential exercise studies published in allegedly asymptomatic patients. Repeat studies after surgery find exercise capacity is actually significantly better. So, many of these patients may have mild symptoms from MR and attribute some fatigue to getting older, but these sequential exercise tests indicate that the fatigue was from the MR.

Dr Adams. I wonder, Pat, if you could comment on the reasons why the replacement rate was greater in patients that were in functional class III–IV. Was this related to pathology, surgical risk, or both?

Dr McCarthy. It's a little of both. It was a group of patients that were, in general, older. On review, the 27 patients with mitral replacement had calcification of the leaflets, many were in their late 70s or 80s. Some had had subacute bacterial endocarditis with extensive leaflet damage. Some needed complex multiple valve or coronary artery bypass operations. Also, the group that were New York Heart Association (NYHA) class 3 to 4 were much more likely to be reoperations. Still, the repair rate even in older patients was very high.

Dr Adams. In a recent editorial written by myself and Ani Anyanwu in the *Journal of the American College of Cardiology*, we discussed Tirone David's publication of his very long-term outcomes in degenerative patients. We pointed out the need to address other processes associated with severe MR, and not just eliminate the MR at the time of surgery. Can you comment on your 100% use of the maze procedure in patients with atrial fibrillation in your series, which is very different than what we see in the Society of Thoracic Surgeons database? Tell us about the keys to achieve the successful results you reported as well—a 90% cure rate of atrial fibrillation in class I patients.

Dr McCarthy. A focus of our approach is to do this procedure very efficiently. Years ago, I switched to cryo-ablation instead of bipolar radiofrequency ablation. It's faster and easier. I have a technique that we're submitting for publication using 3 cryo-ablation lesions to create a box lesion that incorporates the left atrial appendage lesion, a lesion to the mitral valve annulus, and epicardial ablation of the coronary sinus. So, with 3 applications of the cryoprobe you can do the classic left-sided Cox-maze III lesions except for the septum.

Many of the patients had a left atrial only maze. We published our results with that group compared with biatrial lesions. With early referral of asymptomatic patients, there isn't as much tricuspid regurgitation, PA pressures are usually normal, they don't have a dilated right atrium, and those with atrial fibrillation usually had paroxysmal atrial fibrillation. So, for that group of patients a left atrial maze will be successful, because there's no right-sided pathology. Whether the absence of late atrial fibrillation protected them from recurrent MR—I don't know. But atrial fibrillation has been associated with recurrent tricuspid regurgitation in a study from Northwestern last year at the American Association for Thoracic Surgery.

Dr Adams. I must say when I read your paper, I speculated that your success in treating atrial fibrillation did

help the overall results, and the excellent survival you are reporting. Having said that, I'm less convinced about your conclusions regarding the impact of functional class on outcomes. One of the advantages of helping with the American Association for Thoracic Surgery Quality Gateway is that I am on the phone all the time with Gene Blackstone, and I was speaking to him earlier about something else, and ran your results by him, because they puzzled me, as this is the first time symptoms were not implicated in terms of MR outcomes. After looking at your data together, we believe your propensity matching is flawed if you look at the numbers. What I mean by that is you are taking the worst patients from the class I group and you are comparing them to better patients in the class II group, and the best patients in the class III/IV group.

I will give you an example: the survival in the unadjusted class I patients was 92% but, in your propensity-matched class I cohort it was only 87.3%. So, survival in the class I patients, not matched, had to be much greater than 92%. These patients you selected were sicker, and probably older. By comparison, the unmatched class III/IV patients had an unadjusted survival of 75% but in your propensity-matched cohort, the survival rose to 82%. These were the best class III/IV patients being compared with the worst class I patients. I am sure this also happened to some degree in the class II cohort-matching. About a third of the patients from class I and class II were excluded during your propensity matching. I point this out because I do not think we are quite ready to dismiss the outcome penalty of New York Heart Association functional class on survival, based on your data.

Dr McCarthy. I couldn't agree with you more. As they say, the absence of proof is not the proof of absence. My statistician and I have discussed this a few times, and he notes that this comparison is somewhat forced because the groups are so different at baseline. So, in my presentation I wanted to show the absolute difference in survival. In the propensity matching there was a trend toward a difference in survival and some of those patient numbers were pretty low after matching. If we had larger numbers, I'm sure we would have seen the difference.

Now, I have to say that is for NYHA class III and IV patients. For Dr David's paper and for ours, the difference in survival between class I and class II is not different. So we don't think that there's that much of a risk if you wait a little bit until patients get early symptoms. But the take-home message is: Don't wait until the patients are developing more advanced symptoms. Get to them early—either asymptomatic or very early class II-type symptoms.

Dr Adams. I think you are right on this point, Pat. We do not know the impact of the duration of symptoms either, but I am sure this would also influence the outcomes in many patients. I think our main emphasis should remain on interventions on all patients with any symptoms, which is consistent with the guidelines.

Dr McCarthy. I agree. Maurice Sarano wrote a compelling paper about the outcome penalty based on the Mayo Clinic experience between 1990 and 2000. During that decade, beta-blockers were introduced for patients with heart failure, angiotensin-converting enzyme inhibitors, and biventricular pacing. These days patients don't present as late. For example, the ejection fraction difference between NYHA class I and class III–IV patients in our group was only 3%—statistically, but not clinically, different. Comparing results from 1990 to today, it's a whole new world.

Dr Adams. I really commiserate how hard it is to get long-term echo follow-up, and your paper reports an 85% success-rate in getting long-term echo follow-up. Can you comment if you have done a longitudinal analysis in terms of echo results? It is a more valuable data point to have, for instance, an echo that is 7 or 8 years' postoperatively than 6 months' postoperatively. So, how are you going to handle that in your analysis?

Dr McCarthy. We have our database people focus on getting late echoes. An issue we all deal with is that the appropriate use criteria says that patients don't routinely need a follow up echo. I'd love to have them get an echo every year. But if the patient feels well and has no murmur years after repair the cardiologist frequently doesn't order one. There's no universally accepted way to report echo in follow-up. It's like reporting freedom from atrial fibrillation in follow up; it may come and go. In this case a patient may have moderate MR on one echo reading with all later reads being mild MR. We report recurrent MR 2 ways therefore. The group that have more than moderate are more concerning. Typically we wouldn't reoperate or do an intervention for moderate, but we would consider it for 3 or 4+. They likely have an organic lesion of the valve. More than moderate fortunately was very low.

Dr Adams. Pat, I will just finish by saying I know that the coronavirus disease 2019 pandemic has really changed all of our professional lives and taken away some of our usual academic exchange opportunities. It was very enjoyable to spend this time with you in the pursuit of excellence, through our discussion. I think when you are done with all of the analyses and your paper is published, it is going to become another important contribution that will be quoted and referred to often. I just want to congratulate you and your co-authors on this paper.

Dr McCarthy. Thanks, David. I appreciate the comments and we're all thinking of you in New York City during this difficult time.

Dr Adams. Well, we're getting better. Just before we leave, let me open the microphone and maybe Dr Tirone

David can make a comment. Tirone's paper last year looking at his very long-term outcomes is, in my opinion, the true benchmark and we should not leave this session without Tirone making a comment.

Dr Tirone E. David *(Toronto, Ontario, Canada)*. I don't have much to add. Maybe some questions to Patrick. How did you do these operations? Robotic, thoracotomy, sternotomy?

Dr McCarthy. These are old-fashioned sternotomy operations, Tirone. We have submitted a paper about the quantitative algorithm and measured technique that we used to create the proper coaptation without systolic anterior motion.

Dr David. To have 100% freedom from reoperation, and only 1.5% severe MR at 10 years, is going to be very difficult to replicate by minimally invasive approaches. If I'm a patient, and I can read English, I'm going to Google, find your paper, and my dilemma is going to be: should I compromise the quality of my operation for a small scar on my chest?

The other question one is: I am amazed that you have no reoperation at all, because in my hands, preoperative functional class has no effect on the durability of the operation. On survival, yes, it's very important. It's the pathology of the mitral valve that affects long-term outcome. Posterior prolapse very seldom fails; at 20 years maybe 2% to 3% came up with disease elsewhere. In Barlow's with multiple-segment prolapse, they're tougher operations. We are doing more and more on 30-, 40-, and 50-year-old patients and they usually do not have multisegments prolapse. They frequently have more advanced myxomatous degeneration, and repair is much more complicated. And unfortunately, with many more failures—not 0 at 10 years.

Dr McCarthy. About 40% had bileaflet disease or anterior leaflet disease, so most had posterior leaflet disease only. I think it was just chance that the asymptomatic group had zero reoperations. I agree with you, it's progression of the pathology that leads to reoperation, not the patient's symptoms from 10 years earlier. If I look at my results in 20 years like you, then you'll probably see that, but we didn't see it in 10 years. The more advanced pathology likely will lead to more reoperations over time, but it's likely with the early referrals the pathology was at an earlier stage when it was repaired.

I've noticed that the patients with ruptured cords who postponed surgery for years have much more advanced disease and need a more complex repair. The tension on the non-ruptured chords over time contributes to progression of disease.

Dr David. Well, congratulations. These are quite spectacular results.

Dr Y. Joseph Woo *(Stanford, Calif)*. Pat, congratulations again on the outstanding results. I am interested in exploring the topic but in the other direction. You are comparing class I with class II and then to class III. However, if your results are that great in class 1 patients and as you conclude safe, effective, and durable, at what point do we start considering operating on class 1 asymptomatic patients who have, 3+ MR with a clear-cut structural lesion that you know will progress over time?

Dr McCarthy. If they have greater than moderate, then we will consider operating on that group. Most patients, maybe 95%, are compliant and they'll come back in 6 months, so I don't push too hard. I don't know anyone that has good data operating as early as you suggest. Perhaps it will halt progression of the disease and the repairs will be very safe, effective and durable. It's an interesting concept. By the way, Tirone regarding your comment about it being a benchmark for less invasive surgery, it's more important that it's a benchmark for transcatheter procedures. They're facing an extremely high bar with degenerative MR trying to repair or replace the valve.

Dr Matthew A. Romano *(Ann Arbor, Mich)*. Pat, that really was a great presentation. My question is, how do we educate or get this message out? I am continually surprised by how many patients I see in my mitral clinic that have had symptoms for some time, but are ultimately referred by their cardiologist when they are in class III or class IV. I was wondering when I looked at your timeline, it looks like in 2018 your volume dropped off a little bit after a steady increase. Is that reflective that still there's such uncertainty from cardiologists as to when to refer? I think we're potentially missing a huge volume of patients that we could otherwise be helping earlier in their disease and improved outcomes and it is important to get the correct message out.

Dr McCarthy. Matt, the national data would certainly indicate that it has not caught on. I happen to work in an institution where Bob Bonow and Jim Thomas wrote the guidelines. So at Northwestern, and in the region, the cardiologists are well educated about early referrals. We need more publications coming out indicating that it's not just safe for 30 days, but there's great long-term results. That's really the point of this paper.

Dr Romano. The other concern is related to your comment in regard to the transcatheter space and the push to use this technology, and that maybe willing to accept a much lower bar of success as a trade-off for a less-invasive approach.

Dr McCarthy. Well, let's hope not. Any transcatheter technique that decreases your chances for a repair because it damages the valve is contraindicated in young healthy patients.