PAPER

Mixter Lecture: Changing Clinical Practice in Surgery

Irving L. Kron, MD

The purpose of this lecture is to determine how surgical dogmas change. Clearly, change is critical for evolution of surgical technique and concept. The purpose of every academic surgeon, in addition to their teaching and research roles, is to translate basic science principles to clinical care. It is perhaps worthwhile to define dogma as "a principle, belief or idea authoritatively considered to be the absolute truth."[1] To illustrate changing dogmas I would like to use the surgical treatment of heart failure as a model.

Why heart failure? It appears that 5 million Americans are afflicted with 400 000 new cases per year. There is an increasing incidence of heart failure in an elderly population. The annual cost exceeds $10 billion with 75% of the cost owing to hospitalization. Medical therapy, in general, has not been promising particularly for the treatment of ischemic cardiomyopathy. Despite the use of various angiotensin-converting enzyme inhibitors the 2-year mortality approaches 50%.

HEART TRANSPLANTATION

The first dogma worth discussing is the concept of heart replacement, that is, transplantation as the ideal surgical treatment for heart failure. Since its introduction in 1967 by [the late] Dr Christian Barnard, heart transplantation has been the main surgical treatment for heart failure. It is extraordinarily exciting therapy and clearly it works well. At one time at our own institution it was really the only way of treating most forms of cardiomyopathy. Otherwise, patients were relegated to medical therapy. Unfortunately, this dogma had to change purely based on need. There has been a limited number of organ donors. It has become clear that there will never be enough organ donors available for all patients with heart failure.

Dr Lynn Warner Stevenson said it best when she stated "the idea of treating heart failure with transplantation is like treating poverty with the lottery" (oral communication, November 8, 2003). In addition, in patients with ischemic cardiomyopathy, transplantation is far better reserved for patients with idiopathic or dilated cardiomyopathy. A study by Aziz et al[2] demonstrated that those patients who underwent a transplantation for ischemic heart disease had an operative mortality rate equivalent to those who received a transplantation for dilated cardiomyopathy. However, at the end of 10 years only 39% of the patients who underwent transplantation for ischemic cardiomyopathy were alive compared with 80% of the patients who underwent transplantation for dilated cardiomyopathy.[2] Those patients with ischemic cardiomyopathy had other comorbidities that prevented their long-term survival. The best use for resources is reserving heart transplantation for patients who have no other surgical alternatives.

CORONARY BYPASS SURGERY

The next dogma was that coronary artery bypass (CAB) surgery carried a prohibitive risk in patients with ischemic cardiomyopathy. Hochberg et al[3] published a study in 1983 demonstrating that CAB surgery in patients with ejection fractions of less than 20% (normal being 60%-70%) was

Author Affiliations: Department of Surgery, University of Virginia, Charlottesville.

©2005 American Medical Association. All rights reserved.
Downloaded From: http://archsurg.jamanetwork.com/ on 07/08/2015

associated with a prohibitive mortality. The 30-day mortality in this series was 37% and the 3-year survival was only 15%. At that time our institution had a large series of patients treated surgically for ventricular arrhythmias in patients who had left ventricular aneurysms. We had good results with this but had not extended this principle to patients with purely an ischemic dilated ventricle without a discrete aneurysm. Eventually, we were pushed to do this and were surprised to find that the results were really good. We demonstrated in an early series an operative mortality of 2.6%. The 3-year survival approached 90% even though their ejection fraction only increased an average of 8%.[4] Dogma changed here only because of the necessity of offering CAB surgery for patients who had no other alternatives. We subsequently found out that the status of the distal coronary vasculature was clinically important as well. We had previously relied on the presence of ischemia as a good-enough marker for a good result. We found in patients with poor distal vasculature the mortality was prohibitive. This was related to this being a marker for diffuse atherosclerosis.[5]

LEFT VENTRICULAR REMODELING

We became satisfied with the results of CAB surgery in ischemic cardiomyopathy. We were able to demonstrate continued good results and believed at that time the dogma that ventricular size did not matter. We felt if there was evidence of ischemia, CAB surgery alone was all that was needed. Yamaguchi et al[6] disproved this dogma. They reviewed 41 patients undergoing CAB grafting between 1990 and 1995 with ejection fractions of less than 30%. They had good results, with 2 operative deaths and 6 late deaths. They decided to study those patients who were found to have a left ventricular end-systolic volume index greater than 100 mL/m^2. They compared those patients who had the large ventricles with those who had the small ones. The actuarial 5-year survival for the patients with the big ventricles was only 53% whereas those with the smaller ventricles was 85%. More importantly, they found that in the patients with large ventricles only 31% were free of heart failure at 5 years compared with 85% of those with smaller ventricles.[6] This study clearly changed the dogma that the size of the heart did not matter.

The issue was what to do about all this? A remaining dogma was that ventricular remodeling was only possible in patients with discrete aneurysms. If the aneurysmal segment was excluded, the remaining portion of the heart would work more effectively. Dr Vincent Dor originally developed a method of left ventricular aneurysm repair by placing a patch inside the ventricle. He subsequently described 51 patients who had diffuse ischemic cardiomyopathy vs 49 others who had true aneurysms. The hospital mortality was 12% in both groups, but patients with either a large akinetic scar or a true aneurysm did equally well. Therefore, the procedure he developed for aneurysms could be extended to reshape ventricles that did not have discrete aneurysmal segments.[7] This procedure was introduced to us by Dr Gerald Buckberg who popularized this in the United States and convinced us to try this procedure. The issue was, of course, where to place the patch. Buckberg suggested this should be done with the heart beating and then the patch placed within the ventricle at the position where the heartbeat could no longer be palpated. There are some theoretic disadvantages to this in that these patients often have a clot inside their ventricle. Also it is more difficult to sew the patch in patients with the heart beating. We, therefore, compared a series of patients at our own institutions who had the beating heart technique as described by Buckberg compared with simply cross-clamping and using other techniques to determine where the patch should go. We demonstrated equivalent results with no mortality in either group of patients. The mean ejection fraction after both techniques was equivalent at 33%. At least, in our hands, we felt that the beating heart approach was unnecessary for ventricular remodeling.[8]

As mentioned earlier, although Yamaguchi et al[6] had demonstrated that a large heart undergoing CAB surgery did not do as well as a small heart, there certainly had been no demonstration that reducing the size of the heart would add anything to CAB surgery alone. The STICH (Surgical Treatment for Ischemic Heart) trial presently being funded by the National Heart, Lung, and Blood Institute has as one of the hypotheses to be tested this question. The results from this trial are not yet in. We decided to see if we could figure out this answer from our experience. We compared 39 patients who had CAB surgery alone with 56 patients who had CAB surgery and ventricular remodeling in patients with dilated hearts. The preoperative ejection fraction percentage was similar in both groups, that is, in the low 20s. The diameter of the ventricles was equal with a left ventricular end-diastolic diameter of 6.4 cm in both groups. Both groups of patients had equivalent amounts of angina and heart failure. Fortunately, in both groups the hospital mortality was negligible. However, at the end of 1-year follow-up, we noted that the long-term mortality for the group who underwent CAB surgery alone was 5% vs 1.8% for the group who underwent CAB surgery and ventricular remodeling. More importantly, 18% of the group who underwent CAB surgery alone was rehospitalized for heart failure in the follow-up period vs 4% of those in the CAB surgery and ventricular remodeling group ($P<.05$).[9] Changing the size of the heart was superior to CAB surgery alone in patients with ischemic cardiomyopathy and large ventricles.

MITRAL VALVE REPAIR

The final dogma to be discussed is the issue of mitral regurgitations in patients with cardiomyopathy. I was taught during my residency that mitral regurgitation was in fact a good thing in patients with poorly functioning hearts. This belief was based on the fact that patients who had mitral valve replacement often had a worsening of their ventricular function after undergoing a valve replacement. The thought that having a pop-off valve was considered good in these patients because it allowed some of the blood to go backward and reduced stress on the heart. It turns out this dogma not only is incorrect but was also based on faulty science. Patients had worsening of their heart function at the time of valve replace-

©2005 American Medical Association. All rights reserved.
Downloaded From: http://archsurg.jamanetwork.com/ on 07/08/2015

ment because the papillary muscles were removed. The relationship of the mitral valve to the rest of the left ventricle is critically important to maintaining cardiac function. More importantly, mitral regurgitation turns out to be bad in patients with ischemic cardiomyopathy. The presence of mitral regurgitation markedly worsens their outcome.

Dr Steven F. Bolling and colleagues[10] demonstrated that mitral valve repair could be done successfully in patients with very poor cardiac function. He and his colleagues subsequently published articles about patients with end-stage cardiomyopathy who underwent mitral valve repair. He and his colleagues noted a hospital mortality of only 5%. The 2-year actuarial survival was 70%. Most patients at the 2-year follow-up were categorized as having New York Heart Association class 1 or 2 disease (ie, patients with no limitation of activities who have no symptoms from ordinary activities or patients with slight, mild limitation of activity who are comfortable with rest or with mild exertion). This was despite a mean ejection faction of 26%.[10] Bolling et al's patients all underwent mitral valve repair. The results of mitral valve replacement in patients with cardiomyopathy are not so good. I suspect this is owing to the fact that the papillary muscles are frozen and cannot function normally in patients who have valve replacement. We demonstrated similar results in patients with ischemic mitral regurgitation. In our series of patients, we compared valve repairs to valve replacements in patients who have ischemic disease and mitral regurgitation. Both groups were done by the same surgeons. The results were striking. The mortality in the patients who underwent valve repair was only 2% compared with 10% for those who underwent valve replacement ($P<.05$). Clearly, repairing the valve was better for preserving its ventricular function than replacing it.[11]

CONCLUSION

I think it is proper to return to the first dogma—the superiority of cardiac transplantation to other surgical techniques in patients with heart failure. As I mentioned previously, that dogma was discarded basically because there had been a shortage of hearts for transplantation. However, it would be worthwhile to compare the results: transplantation vs these other procedures I have mentioned assuming hearts were available. To do this, we compared 4 groups of patients. We compared UNOS (United Network for Organ Sharing) status II cardiac transplantation patients with patients undergoing CAB surgery for ischemic cardiomyopathy, mitral valve repair plus CAB surgery for ischemic regurgitation, and finally, left ventricular reconstruction that included a few patients undergoing the Batista procedure. The cardiac transplant patients were UNOS status II, that is, these were not the most acutely ill patients. We found that the mortality for the various procedures included heart transplantation at 5.8%, CAB surgery for ischemic cardiomyopathy at 4%, mitral valve repair plus CAB surgery at 6.7%, and finally, left ventricular reconstruction at 4%. Essentially all these procedures had equivalent mortalities. Clearly, transplantation was not superior from that standpoint. We also noted that the 3-year survival, for these various procedures were essential equivalent. The most interesting difference was that of cost. A heart transplantation costs $76 000 despite the fact that these patients were in the hospital a relatively short period. This was owing to the procurement cost of $30 000. The CAB surgery costs $25 000, the mitral valve repair plus CAB surgery costs $32 000; and finally, the left ventricular reconstruction costs $27 000.[12] Clearly alternative procedures in selected patients were at the very least equivalent to cardiac transplantation.

Dogmas continue to be changed. As mentioned earlier, one of the joys of practicing in academic institutions is to have the ability to translate scientific principles into clinical practice. I think Dr Francis D. Moore stated this best with the following quotation:

> A surgical investigator is a bridge tender, channeling knowledge from biological science to the patient's bedside and back again. He traces his origin from both ends of the bridge. He is thus a bastard and is called this by everybody. Those at one end of the bridge say he is not a good scientist, and those at the other say that he does not spend enough time in the operating room. If only he is willing to live with this abuse, he can continue to do his job effectively.[13]

Accepted for Publication: November 26, 2004.
Correspondence: Irving L. Kron, MD, Department of Surgery, University of Virginia, PO Box 800679, Charlottesville, VA 22908 (ILK@virginia.edu).
Previous Presentation: This lecture was presented at the 85th Annual Meeting of the New England Surgical Society; October 3, 2004; Montreal, Quebec; and is published after peer review and revision.

REFERENCES

1. *Stedman's Medical Dictionary.* 27th ed. Baltimore, Md: Lippincott William & Wilkins; 2000:535.
2. Aziz T, Burgess M, Rahman AN, Campbell CS, Yonan N. Cardiac transplantation for cardiomyopathy and ischemic heart disease: differences in outcome up to 10 years. *J Heart Lung Transplant.* 2001;20:525-533.
3. Hochberg MS, Parsonnet V, Gielchinsky I, Hussain SM. Coronary artery bypass grafting in patients with ejection fractions below forty percent. Early and late results in 466 patients. *J Thorac Cardiovasc Surg.* 1983;86:519-527.
4. Kron IL, Flanagan TL, Blackbourne LH, Schroeder RA, Nolan SP. Coronary revascularization rather than cardiac transplantation for chronic ischemic cardiomyopathy. *Ann Surg.* 1998;210:348-354.
5. Langenburg SE, Buchanan SA, Blackbourne LH, et al. Predicting survival after coronary revascularization for ischemic cardiomyopathy. *Ann Thorac Surg.* 1995; 60:1193-1197.
6. Yamaguchi A, Ino T, Adachi H, et al. Left ventricular volume predicts postoperative course in patients with ischemic cardiomyopathy. *Ann Thorac Surg.* 1998; 65:434-438.
7. Di Donato M, Sabatier M, Dor V, et al. Akinetic versus dyskinetic postinfarction scar: relation to surgical outcome in patients submitted to endoventricular circular patch plasty repair. *J Am Coll Cardiol.* 1997;29:1569-1575.
8. Maxey TS, Reece TB, Ellman PI, Kern JA, Tribble CG, Kron IL. The beating heart approach is not necessary for the Dor procedure. *Ann Thorac Surg.* 2003;76: 1571-1575.
9. Maxey TS, Reece TB, Ellman PI, et al. Coronary artery bypass with ventricular restoration is superior to coronary artery bypass alone in patients with ischemic cardiomyopathy. *J Thorac Cardiovasc Surg.* 2004;127:428-434.
10. Smolens IA, Pagani FD, Bolling SF. Mitral valve repair in heart failure. *Eur J Heart Fail.* 2000;2:365-371.
11. Reece TB, Tribble CG, Ellman PI, et al. Mitral repair is superior to replacement when associated with coronary artery disease. *Ann Surg.* 2004;239:671-677.
12. Cope JT, Kaza AK, Reade CC, et al. A cost comparison of heart transplantation versus alternative operations for cardiomyopathy. *Ann Thorac Surg.* 2001; 72:1298-1305.
13. Moore FD. The university in American surgery. *Surgery.* 1958;44:1-10.

©2005 American Medical Association. All rights reserved.
Downloaded From: http://archsurg.jamanetwork.com/ on 07/08/2015