Enthusiasm Tempered

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In 1954, Charles Hufnagel, Proctor Harvey, and colleagues published their classic description of the first effective surgical treatment of end-stage aortic insufficiency, or indeed of any form of advanced valvular insufficiency. First at the Peter Bent Brigham, they had worked long on the matter, later moving to Georgetown University Medical Center. There they developed a clever and elegantly simple approach to the task of supporting the overloaded left ventricle within the particular anatomic and physiological allowances of valvular aortic insufficiency. The challenge, which was met with gratifying effectiveness, was to interrupt the aortic outflow without the benefit of circulatory support machinery not then available, and to then interpose a prosthetic valve at a point where regurgitant flow could be arrested. The now famous solution was to accept a remedy not entire, interrupting the aorta distal to the left subclavian artery. As the flow to the arch vessels was not interrupted, the simple surgical interposition of the caged ball valve device in the descending aorta was understandably well-tolerated. The relief of regurgitation was thus only partial, but proved to be sufficient to provide meaningful palliation. In fact, the first patient survived for 7 years. Other physiological issues, such as the adequacy of the remaining compliance chamber or the effect on coronary blood flow did not dictate the clinical response to the treatment.

Later was to come the development of circulatory support machines and with them techniques for surgery on the arrested heart with full exposure of the valvular anatomy for repair and replacement. The principle of orthotopic implantation of prosthetic valves then became the dominant, if not ideal, approach. There were a number of interesting proposals for circulatory valve devices through the years, but until the age of interventional cardiology, when “transcatheter” device development exploded, the idea of “percutaneous” repair, then replacement of a cardiac valve, did not appear realizable. First, of course, was the development of the balloon catheter with variant designs successfully applied to the dilation of stenotic valves. Then, in the mid to late 1980s, cardiovascular medicine was forever redirected by the advent of the vascular metal stent in all its forms. The notion that the stent could be more generally characterized as a scalable delivery platform for valves or drugs, for example, was immediately apparent to its developers.

Soon after, in 1992, Andersen et al reported the first practical experiment in which a stent-mounted pig valve was implanted by balloon catheter. In 2000, Bonhoeffer et al reported successful pulmonic valve implantation in a lamb model of a refined percutaneous valve consisting of a tissue valve harvested intact from bovine jugular vein, then affixed within a balloon-expandable metal stent. This technique was later successfully applied in failing patients to the incompetent conduits originally placed for the treatment of congenital pulmonary atresia. Finally, came the signal report by Cribier et al of the implantation of a stent-mounted biological valve in a patient with inoperable critical aortic stenosis in April of 2002.

Today, work on the “non-surgical” or “percutaneous” repair or replacement of cardiac valves is proceeding at a pace that reflects intensifying professional and commercial interest. Characteristically, the pace of device development has followed the development of permissive technologies, most accountable of these being the vascular stent. However, the knowledge—anatomic, physiological—that supports this endeavor has lagged behind. In their work, Hufnagel, Harvey, et al had to take account of the exact physiology of the specific lesion (aortic insufficiency), and during device implantation they could not allow the interruption of cerebral perfusion by their surgical manipulations. No one had ever proposed to interrupt the central circulation or to substitute for an anatomical valve, and nothing could be taken for granted. In some sense, in the field of percutaneous heart valve repair and implantation, we find ourselves standing on similar ground.

Numerous developments in interventional cardiology have turned aside doubt and even incredulity in their paths to success. We may be forgiven then for viewing the percutaneous valve enterprise with the same sort of enthusiasm and confidence inherited from balloon and stent therapy. We may have the appetite to swallow the propositions whole, but it is early in the course of this story and is still useful to inquire why, indeed, do we need percutaneous valve therapy? By some account, surgical valve therapy has an enviable track record. In the UK Heart Valve registry, the mortality rate for aortic valve replacement in octogenarians was still only 6.6% at 1 month and 11% at 1 year. Postoperative morbidity is less well understood, but advocates of percutaneous aortic valve replacement therapy must begin by acknowledging a high performance standard in searching its justification.

Defining the scope of heart valve disease that might benefit from percutaneous valve therapy is difficult; the magnitude of what is treated obscures a large group of patients who are not treated out of an appreciation for the limited value of therapy.

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when the risks may be high, or by consequent preferences of practitioners in a practice environment of increasing scrutiny. In one sense then, as much as by the range of patients who are treated for advanced valve disease, the field is defined in large part by what we don’t do. Approximately 90,000 open heart valve surgeries are performed annually in the United States. Those valve disease patients excluded from this cohort include a number of groups. The elderly are often proposed by mere age or common comorbidities to be unacceptable for surgical repair. There are treatment denials to other high-risk or otherwise terminal patients. The risk and morbidity in pediatric or adult congenital lesions is often unacceptable. Valve surgery is resource-intensive and therefore limited or not available in many parts of the world. Thus, although impossible to quantify, there is reason to expect a substantial unmet need for valve repair or replacement that could be done with lower risk and cost.

Beyond this, there are subtle potential advantages for the lowering of the formidable morbidity/risk threshold for treatment traditionally imposed by the surgical enterprise. Assuming reliable techniques for percutaneous valve therapy, treatment might be offered earlier in the course of clinical decompensation with improved outcome and more effective palliation. Current percutaneous valve designs, being chiefly stent-mounted without a surgical sewing ring, also offer potentially superior hemodynamics as compared with traditional surgical prosthetic valves. Finally, because of the broad scalability of percutaneous valve designs, novel applications may be expected to expand the clinical range for therapy, including valves for surgical conduits or to treat venous insufficiency.

Accepting the mission, workers in the field have begun from a fairly complete knowledge of device design that integrates the known technologies of stents and balloon catheters, but they have had to confront a surprising lack of fundamental anatomic and physiological intelligence about the nature of failing heart valves. Further, this essential knowledge appears to be particular not just to the specific valve in question, but also to the specific lesion. For example, we have found that chronic aortic stenosis seems to cause expansion of the sinuses of Valsalva and descent of the central coaptation point of the leaflets, whereas the left ventricular outflow tract elongates but does not expand. These influences have a permissive effect on the implantation of a percutaneous aortic valve, which must seat in the left ventricular outflow tract but not impinge on the coronary ostia. By contrast, the left ventricular outflow tract does expand significantly in chronic aortic insufficiency, and the relationship between the level of leaflet coaptation and the level of the coronary ostia is not certain to allow stented valve implantation without threat to coronary perfusion. A clear understanding of the dimensions can drive the tactical approach to implantation. For example, a stented (and strutless) valve 20 mm in diameter (ignoring the mass of biological membrane) could have a theoretical valve area of about 3.1 cm². In practical experience, implanting percutaneous stented valves in chronic aortic stenosis reported by Cribier et al. and others, the effective valve area is typically 1.7 cm²; and the sonographic appearance of this implant indicates a small profile within the expanded plane of the sinuses clearly distant from and no conceivable threat to the coronary ostia. With knowledge of such generous performance margins, the a priori notion that the stent profile should fully efface the aortic valve ring to achieve an effective hemodynamic profile is obviously naïve, and designers can use less demanding criteria in approaching aortic stenosis.

Much of our intelligence for valve therapy has been based in animal research that, for surgical valve replacement, has naturally involved orthotopic implantation, allowing reasonable confidence in the observations in chronic animal subjects. In contrast, percutaneous valve research depends more directly on the features of the mature natural disease state, for which there are no substantial animal models. Furthermore, Food and Drug Administration regulatory guidance for required animal research is oriented to surgical prosthetic valves and is not appropriate to the percutaneous valve enterprise. We can expect that these matters will be in flux for some time.

In approaching the pulmonary position and related surgical conduits, Boudjemline and co-workers have previously reported the anatomic difficulties of stented valve implantation in markedly expanded pulmonary outflow tracts. Using an ovine model, they reported success in a 2-stage procedure in which a special toroidal nitinol “downsizing” stent was first deployed, and the stented valve was later deployed within the central reduced conduit of the first stent. Although this may not be the only or final solution to the specific problem of the pulmonary position, it illustrates the very kind of thinking that will be needed if percutaneous valve implantation is to become a reliable and accepted form of therapy.

A growing series of reports reflect the encouraging march of developments in the field. A number of remaining issues seem increasingly likely to be solved. Paniagua and colleagues have developed a unique low-mass membrane valve scalable to any size. We have reported the robust mechanics of this stented valve prototype tested in a flow loop device, with a negligible antegrade gradient and minimal leak at high static pressures, hinting that valves of this general design will likely comply with current regulatory requirements based on surgical valve standards. The delivery approach for the percutaneous valve catheter systems has been limited by the large caliber of the current designs; the initial implantations by Cribier et al. required a 24 Fr sheath for transseptal delivery of the stented valve to the aortic position via the more accommodating femoral vein pathway. Progress has been made in this regard as technical designs have improved. Paniagua et al. have reported successful human retrograde aortic valve implantation with an 18 Fr delivery system, and Cribier’s group has also succeeded in a number of retrograde implantations. Self-expanding stent frames are lower in profile than balloon-expanded designs. Boudjemline et al. have described 16 Fr delivery, and other groups have experimented with 10 Fr designs.

Accurate and secure deployment will remain a significant issue for these procedures and will likely depend on effective imaging techniques. The early success of Cribier et al. with implantations in calcific aortic stenosis depended largely on
fluoroscopic visualization of the calcified valve plane as a reference mark for deployment. Other non-calcific valve lesions may well require more than radiographic imaging. Kuehne et al\textsuperscript{16} reported successful deployment guidance of stents in valve positions by live magnetic resonance imaging techniques, and others have experimented with intracardiac echocardiography. Initial deployments in human subjects were troubled by dislodgement of the valve implants, partly as a result of adapting available vascular stent technology. Security of implantation will likely improve with stent frames designed to the demands of high force and large diameter. Finally, as indicated by the substantial early mortality in the first human implantations, the patients that can be justifiably submitted to experimental valve procedures are likely to be profoundly ill and at the limit of physiological reserve. Such patients may benefit from temporary circulatory support devices that might allow for a more generous dwell time of the valve device across the valve tract for careful and accurate deployment while the heart is unloaded and the circulation is fully supported.

We can hope and even expect that progress will continue to carry us to the practical realization of reliable and effective percutaneous valve therapy, but many questions remain. In aortic valve replacement, for example, some have asserted that a filter will need to be interposed to protect the cerebral circulation from embolic debris from the degenerate valve; others have proposed devices to excise the native valve before prosthesis implantation. Experience in interventional cardiology tells us that we cannot presume; what appears formidable may prove forgiving, and unforeseen setbacks will doubtless occur. A spirit of enthusiasm tempered with humility will serve us in this enterprise.

Lest we forget, our surgical colleagues are also hard at work to advance the technology of valve surgery. Many of the technical developments and the insights used in percutaneous valve experimentation can be and have been applied to the surgical procedure in both experimental and practical efforts. Improved designs of surgical prosthetic valves have enhanced hemodynamic performance by reducing the supportive structures of the valve. Development efforts are being directed toward surgical valves that can be fixed in place without suturing, in the manner of a self-expanding stent valve. Combined with “limited access” surgical approaches and perhaps even percutaneous circulatory support devices, the “risk tax” for surgery may fall for even high-risk patients. We know that successful surgical cardiac valve repair and replacement has been performed for about 50 years. Even in high-risk and elderly patients, the track record is excellent, reinforcing surgery as the gold standard where it is reason-ably available. Thus, in setting goals for the development of percutaneous heart valve procedures, we must acknowledge that standards for performance and clinical effectiveness will be high, and we must aspire to a worthy form of treatment, not just a crude form of palliation.

On September 12, 1952, Martina Hall became the first patient to receive the Hufnagel procedure for severe aortic insufficiency. She lived a productive life in the 7 years beyond her surgery. This stunning success will not soon be matched by current percutaneous aortic valve procedures. We have a long way to go.

References

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