Indications for aortic aneurysmectomy: Too many variables and not enough equations?*

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Endografting for treatment of thoracic aortic pathology continues to gain popularity; in some countries, endovascular aortic repair numbers now exceed open surgery cases. The skills and understanding of open surgical teams are not always translated into endovascular interventions, which may be led by a cardiologist or vascular surgeon with little knowledge of thoracic pathology. The indications for intervention on the dilated aorta continue to be debated despite volumes of literature and multisocietal guidelines. The challenge of making a binary decision in the face of competing continuous risks depends on a best guess as to when the risk of the natural history of the disease exceeds that of the operation. Unfortunately, we have more information about average risk than actual (patient-specific) risk, and only for some of the variables determining those risks. Individual patient-specific operative risk can be calculated for some procedures by means of the Society of Thoracic Surgeons database, although surgeon-specific risk models are really required. On the other side of the balance, aortic dissection and rupture represent material failure of the aortic wall when tensile stress exceeds tensile strength. When framed in this way, it is not surprising that diameter is imprecise, as this is only one of the variables in the law of Laplace. The circumferential (hoop) stress is the product of radius *and* intraluminal pressure, divided by wall thickness. We also have no good measures of the material properties of the wall that determine strength, although a great deal of attention has been paid to the genetic markers for aortic wall abnormalities. Other factors, such as smoking or poorly controlled hypertension, likely should enter into our clinical assessment because they impact wall strength as well. For now, discussions with patients should be framed with all these elements in mind. (J Thorac Cardiovasc Surg 2013;145:S126-9)

"No surgeon should approach the victim of his operation without a sacred dread and reluctance."

John Hunter¹

The issue of indications for intervention on the dilated aorta might be considered settled. It would be difficult for anyone to add to the scholarly dissertation on the subject by Eleftheriades delivered at the Aortic Symposium just 2 years ago,² and guidelines for intervention have been established by the American Heart Association in partnership with multiple organizations, including the American College of Cardiology, the Society of Thoracic Surgeons (STS), and the American Association for Thoracic Surgery.³ Still, in practice there continues to be a remarkable degree of debate about whether to treat, case by case and provider by provider.

How can we explain this phenomenon and, more importantly, chart a course of discovery to address what is evidently still an unmet need? How can there remain so much uncertainty?

Fundamentally, we are faced with the unsatisfying and inescapably imperfect challenge of making a binary decision in the face of competing continuous risks. By first principles, surgery is indicated when the risk of the natural history of the disease exceeds that of the operation (Figure 1). The ideal would be, in each individual case, to intervene at the exact moment that these lines cross. Unfortunately, we have more information about average risk than about actual (patient-specific) risk, and that only for some of the variables in the relevant equations. As a consequence, any broad guidelines are fated to be at once overinclusive (recommending surgery for patients when it is not in their best interest) and underinclusive (failing to recommend surgery when in fact it should be performed). Nowhere is this more apparent than in the case of aortic replacement to prevent dissection.

Some progress has been made in the effort to calculate individual patient-specific risk through the efforts of the STS database workforce. Although both patient-related and surgeon-specific factors play a role in determining clinical outcomes, as do systems factors, the STS has leveraged the enormous size of the national database to enable custom estimation of operative risk for an individual patient by evaluating a finite—and inescapably imperfect—number of objective variables for certain specific procedures. In

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FIGURE 1. The recommendation to proceed with surgical intervention or continue to observe should be made on the basis of consideration of all of the data elements entering into the competing risks.

time, the requisite models will likely be built for aortic procedures as well, helping us to fill in the blanks on the operative risk side of the equation. This too will be imperfect; in reality, what is needed are surgeon-specific risk models for any given procedure. This is not statistically possible with any degree of precision for all but a very few surgeons' practices. In the meantime, we will likely continue to rely on case volume as an imperfect surrogate for high-quality surgery. There will never, however, be a substitute for knowledge of actual outcome data, because most of us feel that our own results surpass those reported by others. The risk is a steady drift toward an increasingly aggressive surgical posture. The only practical solution is ruthless honesty and brutal self-reflection: one must know one's own outcomes.

What about the other side of the balance, the risk posed by the natural history of the disease? On reflection, it is really no surprise that aortic diameter is such an inadequate predictor of outcome. Aortic dissection and rupture represent material failure of the aortic wall, when tensile stress exceeds tensile strength. Reframing the matter in these broader terms may lead us to a more comprehensive understanding of the risks of the disease.

Short of a detailed definition of local strain—a worthy but as yet elusive goal—we generally rely upon the law of Laplace to estimate circumferential (hoop) stress in a vessel wall: $\text{Wall tension} = (\text{Pressure})(\text{Radius})/M$, where M represents wall thickness. Even with this imprecise measure, however, we generally take into account only 1 of the 3 variables. No doubt this is because the diameter is the parameter that we can most easily measure. Intraluminal pressure is dynamic and seldom available for a retrospective clinical study, and only recently have imaging modalities become precise enough to consider measuring wall thickness in vivo.

Despite its limitations, aortic diameter has proved remarkably useful. Perhaps this is the reason we have clung

to it in the past. In their seminal study of the natural history of thoracic aortic aneurysms, Joyce and colleagues⁴ noted that patients with a thoracic aortic diameter exceeding 6 cm were at particular risk for catastrophe. Numerous more detailed analyses have since emanated from Elefteriades' group at the Yale Center for Thoracic Aortic Disease⁵⁻⁸; remarkably, the apparently critical diameter of 6 cm remains true to Joyce's predictions. At the same time, it is also increasingly clear that size criteria are insufficiently discriminating in the individual case. It is now well documented that aortic dissections can occur at diameters less than 5 cm even in the absence of defined genetic syndromes.⁹

Among the difficulties in using aortic diameter as a criterion for intervention, the risk of complications cannot be calculated from observations of the dissection population alone (the numerator) without knowledge of the overall population at risk (the denominator).¹⁰ In addition, the focus on aortic diameter may distract from the other factors impacting wall stress: the risk of mechanical failure of the aortic wall is also defined by intraluminal pressure (blood pressure) as well as the intrinsic properties of the aortic wall such as thickness, distensibility, elasticity, and stiffness. Evidence of the importance of blood pressure can be found in the well-recognized phenomenon of aortic dissection among weight lifters.^{11,12}

With regard to the material properties of the wall itself—its strength—a great deal of attention has been paid to genetic markers for aortic wall abnormalities such as are found in Marfan or Loeys-Dietz syndromes or families with mutations in *MYH11*, *ACTA2*, or *SMAD3*.¹³ Indeed, the previously mentioned interventional guidelines specifically address the indications for intervention in the presence of these conditions. It is worth remembering, however, that the syndromes are just markers for vulnerabilities in the aortic wall and are not operative indications in and of themselves. The relevance of framing the discussion more broadly is that it may help us to remember to enter factors such as smoking or poorly controlled hypertension into our clinical assessment. The relevance of this distinction is that, for example, arterial hypertension is a particularly bad problem in that it influences not only stress—as noted—but also, if longstanding, wall strength as well. There is a clinically demonstrable impact of chronic lung disease and smoking as risk factors for aneurysmal degeneration and catastrophe.^{14,15} It could be argued that, just as aortic diameter thresholds for intervention are lower in the presence of genetic syndromes, similar guidelines indicating enhanced vulnerability should be codified for current smokers or those with poorly controlled hypertension, given the much higher prevalence than genetic syndromes of these risk factors. Currently neither in discussion with patients nor in formal clinical guidelines is it likely that different

thresholds for intervention that are based on these factors are considered in the same way as for genetic conditions.

Clearly the greatest need is for means of direct assessment of intrinsic material properties in vivo as well as of wall stress, so that this information can be entered into the recommendations for clinical management. Challenges include the inhomogeneous composition of the aortic wall, which may lead to nonlinear stress-strain relationships,¹⁶ not to mention the impact of residual strain in the wall itself.¹⁷ Some work has been done measuring the strength of the wall in vitro.¹⁸⁻²¹ These advances, however, have not yet been translated into clinical practice.

Finally, in any discussion about clinical decision making, something should be said about human decision making in general and its implications both for surgeon and patient preference. Although we, as surgeons, may find it appealing to trust our gut feelings, there is a considerable body of evidence demonstrating that human beings are particularly poor intuitive statisticians and are remarkably poor at assessing competing risks.²² In the interest of cognitive efficiency, we apply heuristics and are subject to predictable, systematic biases. We are good at estimating the mean but tend to overestimate the frequency of events. We underestimate high correlations and overestimate low correlations. We are good at identifying salient cues and identifying patterns, almost to a fault, sometimes even when the cues are misleading or misinterpreted or the patterns do not exist. Our judgments are affected by what we wish to be true or false. As such we are subject to fixation, tunnel vision, and confirmation bias. Taken together the implication is that we should be cautious about our seat-of-the-pants assessments and should avail ourselves of objective data (such as the STS On-Line Risk Calculator) whenever possible.

The implications for patients are equally profound. Arguments for presenting the data objectively and leaving the decision entirely in the hands of the patients in the interest of so-called “patient-centered decision making” run the risk of abdicating our role as professionals and short-changing the individuals we are here to serve. Patients too are subject to cognitive traps, including overvaluing short-term gains over long-term benefits, magnifying small risks and minimizing larger ones, and being unconsciously drawn to focus on positive outcomes without accounting appropriately for negative ones. Perhaps even more relevant to the issue of aortic disease, human beings are driven to take action to eliminate even a small risk, particularly if the consequences of failing to act are vivid. It is no wonder then that a patient who arrives in the office having been told by another clinician that he has a “time bomb” in his chest may be particularly resistant to suggestions that serial observation of his mild aortic dilatation would be appropriate. This is not an argument for paternalism; our role should be to assist our patients in charting a course of action consistent with their true preferences

by actively framing the discussion in a manner that facilitates rational decision making.

In summary, despite herculean efforts to develop guidelines for prophylactic intervention on the ascending aorta, debate continues both in the literature and in the clinic. Criteria derived from aortic diameter are imperfect, perhaps not surprisingly given that diameter represents only one of the parameters defining the relative risk of rupture or dissection and ignores other factors contributing to outcome. Efforts should be made to fill these knowledge gaps. In the meantime, discussions with patients should be framed with all the relevant elements in mind—the risk of the prophylactic operation for this patient in your hands and in your institution versus the risk of complications given the patient’s blood pressure, lifestyle, and profession, as well as any data shedding light on the material properties of the aorta.

References

- Hunter J. Lectures on the principles of surgery. In: Palmer JF, ed. *The Works of John Hunter F.R.S. with Notes*. Vol 1. London: Longman Rees, Orme, Brown, Green, and Longman; 1835:210.
- Elefteriades JA. Indications for aortic replacement. *J Thorac Cardiovasc Surg*. 2010;140(6 Suppl):S5-9; discussion S45-51.
- Hiratzka LF, Bakris GL, Beckman JA, Bersin RM, Carr VF, Casey DE Jr, et al. 2010 ACCF/AHA/AATS/ACR/ASA/SCA/SCAI/SIR/STS/SVM guidelines for the diagnosis and management of patients with thoracic aortic disease: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines, American Association for Thoracic Surgery, American College of Radiology, American Stroke Association, Society of Cardiovascular Anesthesiologists, Society for Cardiovascular Angiography and Interventions, Society of Interventional Radiology, Society of Thoracic Surgeons, and Society for Vascular Medicine. *Circulation*. 2010;121:e266-369. Erratum in: *Circulation*. 2010;122:e410.
- Joyce JW, Fairbairn JF 2nd, Kincaid OW, Juergens JL. Aneurysms of the thoracic aorta: a clinical study with special reference to prognosis. *Circulation*. 1964;29:176-81.
- Coady MA, Rizzo JA, Hammond GL, Kopf GS, Elefteriades JA. Surgical intervention criteria for thoracic aortic aneurysms: a study of growth rates and complications. *Ann Thorac Surg*. 1999;67:1922-6; discussion 1953-8.
- Coady MA, Rizzo JA, Hammond GL, Mandapati D, Darr U, Kopf GS, et al. What is the appropriate size criterion for resection of thoracic aortic aneurysms? *J Thorac Cardiovasc Surg*. 1997;113:476-91; discussion 489-91.
- Davies RR, Goldstein LJ, Coady MA, Tittle SL, Rizzo JA, Kopf GS, et al. Yearly rupture or dissection rates for thoracic aortic aneurysms: simple prediction based on size. *Ann Thorac Surg*. 2002;73:17-27; discussion 27-8.
- Davies RR, Gallo A, Coady MA, Tellides G, Botta DM, Burke B, Coe MP, Kopf GS, Elefteriades JA. Novel measurement of relative aortic size predicts rupture of thoracic aortic aneurysms. *Ann Thorac Surg*. 2006;81:169-77. Erratum in: *Ann Thorac Surg*. 2007;84:2139.
- Pape LA, Tsai TT, Isselbacher EM, Oh JK, O’gara PT, Evangelista A, et al. Aortic diameter ≥ 5.5 cm is not a good predictor of type A aortic dissection: observations from the International Registry of Acute Aortic Dissection (IRAD). *Circulation*. 2007;116:1120-7.
- Sundt TM 3rd. Replacement of the ascending aorta in bicuspid aortic valve disease: where do we draw the line? *J Thorac Cardiovasc Surg*. 2010;140(6 Suppl):S41-4; discussion S45-51.
- Elefteriades JA, Hatzaras I, Tranquilli MA, Elefteriades AJ, Stout R, Shaw RK, et al. Weight lifting and rupture of silent aortic aneurysms. *JAMA*. 2003;290:2803.
- Hatzaras IS, Bible JE, Koullias GJ, Tranquilli M, Singh M, Elefteriades JA. Role of exertion or emotion as inciting events for acute aortic dissection. *Am J Cardiol*. 2007;100:1470-2.
- Milewicz DM, Regalado ES, Guo DC. Treatment guidelines for thoracic aortic aneurysms and dissections based on the underlying causative gene. *J Thorac Cardiovasc Surg*. 2010;140(6 Suppl):S2-4; discussion S45-51.
- Juvonen T, Ergin MA, Galla JD, Lansman SL, Nguyen KH, McCullough JN, et al. Prospective study of the natural history of thoracic aortic aneurysms. *Ann Thorac Surg*. 1997;63:1533-45.

15. McKellar SH, Michelena HI, Li Z, Schaff HV, Sundt TM 3rd. Long-term risk of aortic events following aortic valve replacement in patients with bicuspid aortic valves. *Am J Cardiol*. 2010;106:1626-33.
16. Gasser TC, Ogden RW, Holzapfel GA. Hyperelastic modeling of arterial layers with distributed collagen fibre orientations. *J R Soc Interface*. 2006;3:15-35.
17. Sundt TM 3rd. Residual strain in the aorta. *J Thorac Cardiovasc Surg*. 2006;131:1420-1.
18. Okamoto RJ, Wagenseil JE, DeLong WR, Peterson SJ, Kouchoukos NT, Sundt TM 3rd. Mechanical properties of dilated human ascending aorta. *Ann Biomed Eng*. 2002;30:624-35.
19. Adham M, Gournier JP, Favre JP, De La Roche E, Ducerf C, Baulieux J, et al. Mechanical characteristics of fresh and frozen human descending thoracic aorta. *J Surg Res*. 1996;64:32-4.
20. Vorp DA, Schiro BJ, Ehrlich MP, Juvonen TS, Ergin MA, Griffith BP. Effect of aneurysm on the tensile strength and biomechanical failure of the ascending thoracic aorta. *Ann Thorac Surg*. 2003;75:1210-4.
21. Koullias G, Modak R, Tranquilli M, Korkolis DP, Barash P, Elefteriades JA. Mechanical deterioration underlies malignant behavior of aneurysmal human ascending aorta. *J Thorac Cardiovasc Surg*. 2005;130:677-83.
22. Plous S. The psychology of judgment and decision making. New York: McGraw-Hill; 1993.