Commentary: Preventing the virulent lethality of ascending aortic aneurysm

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Czerny and colleagues\(^1\) have provided a thoughtful, insightful review of guidelines for intervention for ascending thoracic aortic aneurysm (TAA).

Czerny and colleagues\(^1\) have, appropriately, shined a focus on aortic length (annulus to base of innominate artery), on which our group has been concentrating as well.\(^2\) Length has the distinct advantage that it does not change at the moment of aortic dissection. So, in contrast to diameter (which does change acutely), the length we see after dissection was the length just before dissection. This constant nature of aortic length makes it ideal as a variable for evaluation as an intervention criterion.

Two fundamental issues regarding further refinement of surgical intervention criteria are brought to mind by this overview:

1. “Natural history of TAA” is becoming no longer discernible. Heisenberg’s uncertainty principle tells us that when a particle physicist tries to locate an electron, the very process of measurement influences the localization\(^3,4\) (Figure 15). In other words, the process of measurement disturbs the item being measured. We face a similar conundrum in care of the thoracic aorta. In coming to understand the behavior of the aorta, we have implemented preemptive surgical therapy that no longer allows the natural history to be expressed. We operate before the aorta has a chance to dissect. Many of us now operate at 5.0 cm, following an evidence-based “left shift” toward preemptive surgery at smaller aortic diameters than before.\(^5\) So, we are now preempting the natural behavior of TAA, no longer allowing the aorta the opportunity to dissect. Thus, for patients with a diagnosed TAA, the natural history is no longer fully in evidence. The days of observation of TAA into the now known “danger zone” are behind us.

2. Acute aortic dissection cases pose their own natural history dilemmas. So, our main opportunity to observe natural history of TAA is found in previously undiagnosed patients who present with sudden, unexpected type A aortic dissection. But, from a natural history standpoint, these patients are problematic. First, we do not know the date of onset of the aneurysm, so calculation of yearly event rates is hampered. Second, we do not know the size of the aneurysm just before it dissected, obfuscating development of intervention criteria. It is now becoming clear\(^7,8\) that the aorta grows abruptly at the moment of aortic dissection by approximately 8 mm in our calculations. These calculations are based on those few patients who, fortuitously, happened to have a computed tomography scan for other reasons (usually for surveillance of lung nodules) in close temporal proximity to the time of onset of their aortic dissection (Figure 2). So, yearly growth rate and exact aortic size at the moment of aortic dissection are troublesome from an investigational standpoint.
Bespoke management based on molecular genetics is rapidly permitting personalized, data-driven aortic care, with a separate intervention size criterion for each specific mutation. A size “timeline” for such intervention is presented in Figure 3, A. This molecular-based guidance will become more prevalent, as new causative genes are discovered each year. Our suspicion is that, over the next 5 to 10 years, the majority of aortic root and ascending aortic aneurysms will be found to be associated with specific novel genetic mutations.

Another use of molecular data arises from information about the common age at which dissection occurs in specific genetic syndromes (Figure 3, B). Such precision genetics-based age data can help to inform clinical decisions, because age at dissection tends to cluster for each specific genetic variant.10

While we pursue and encourage research into other non-size criteria for surgical intervention (eg, biomarkers, artificial intelligence), no advances seem currently “ready for prime time.”11-13

Besides fine-tuning criteria for surgical intervention, perhaps most important life-saving advance would reside in the diagnosis of silent TAAs.14-16 If we can diagnose the asymptomatic aneurysm carrier in the general population, even our present intervention guidelines will keep him/her quite safe. Diagnosis of asymptomatic carriers probably represents the most potentially impactful means to protect lives from the virulent lethality of TAA.

References
FIGURE 3. A, Size “timeline” for intervention based on specific causative mutation. Reproduced with permission from Faggion and colleagues.9 B, Schematic representation of genetic mutations with age and ascending aorta diameter at dissection. The widening of the circles/lines represents standard deviation in terms of age and diameters. Data are obtained from studies included in the systematic review. No numeric data were available for patients affected by aortic dissection regarding the genes NOTCH1 and MFAP5, and patients with MAT2A mutation did not experience aortic dissections. Reproduced with permission from Mariscalco and colleagues.10