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Advances in surgical thresholds for ascending aortic aneurysms: an expert perspective

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Abstract

The ascending aortic aneurysm represents a critical clinical concern due to its potential for catastrophic complications. With global demographic shifts toward aging populations, the incidence of ascending aortic aneurysms is projected to rise significantly. This brief perspective examines the evolution of our understanding regarding the natural history of ascending aortic aneurysms and the refinement of surgical intervention criteria over time. We discuss the transition from simplistic diameter-based metrics to multidimensional assessment approaches that consider patient-specific factors, including anatomical variations, biomechanical properties, and genetic predispositions. Recent paradigm shifts, such as the recalibration of diameter thresholds from 5.5 cm to 5.0 cm and the integration of volumetric analysis, highlight the field's progression toward more precise risk stratification. This paper aims to provide clinicians with a contemporary framework for surgical decision-making while identifying promising avenues for further refinement of intervention strategies.

Keywords: Aortic aneurysm, surgical indicator, natural history

INTRODUCTION

The ascending aortic aneurysm represents a critical focus in cardiovascular medicine due to the potentially catastrophic consequences of aneurysmal complications. As global populations continue to age, the prevalence of ascending aortic aneurysms is anticipated to increase, presenting heightened clinical challenges. Recent compelling evidence has demonstrated that chronological age alone constitutes an inadequate metric for surgical risk assessment. Carefully selected elderly patients with threatening aortic aneurysms can derive significant benefit from surgical intervention despite advanced age[1].

The fundamental question that continues to challenge clinicians remains: What constitutes the optimal timing for intervention? This perspective aims to provide an overview of the evolution in our understanding of the natural history of ascending aortic aneurysms and the progressive refinement of surgical intervention criteria, integrating historical perspectives with contemporary evidence-based approaches.

Historical development of surgical standards

Systematic investigation of surgical standards for aortic aneurysms began with the landmark study by Joyce *et al*. in 1964[2]. This pioneering research examined the natural history of 107 patients with untreated thoracic aortic aneurysms, revealing a significant survival decline when aortic diameter exceeded 6 cm[2]. This observation established the foundation for diameter-based intervention criteria that would guide clinical practice for subsequent decades.

A significant advancement occurred in 1997 when Elefteriades initiated a comprehensive, ongoing research program on the natural history of thoracic aortic aneurysms. Their initial studies determined that the median diameter at which rupture or dissection occurred was 6.0 cm for ascending aortic aneurysms and 7.2 cm for descending aortic aneurysms[3]. This analysis yielded a crucial insight: if the median diameter at catastrophic complication were used as the intervention threshold, half of all patients would suffer severe consequences before surgical intervention. Consequently, they proposed 5.5 cm as an appropriate threshold for elective resection of ascending aortic aneurysms. This standard was subsequently adopted by the American Heart Association (AHA) guidelines in 2010 and the European Society of Cardiology (ESC) guidelines for aortic disease management in 2014.

Individualization of surgical criteria: consideration of patient body size

Recognizing the limitations of a "one-size-fits-all" approach based solely on absolute aortic diameter, Zafar *et al*. introduced the concept of aortic height index in 2018[4]. This innovative approach incorporated patient height as a factor, enabling more individualized surgical decision-making that accounts for individual body proportions[4]. This represented a significant progression from simple diameter-based criteria toward more nuanced, patient-specific risk assessment. Body size, particularly height, as an important consideration in surgical decision-making has been formally endorsed by recent guidelines, including the 2024 European Association for Cardio-Thoracic Surgery/Society of Thoracic Surgeons (EACTS/STS) Guidelines[5] and the 2022 American College of Cardiology (ACC)/AHA Guidelines[6].

Importance of aortic length

Working with Dr. Elefteriades, Zafar Mohammad conducted a systematic review of Yale's aortic data, establishing an elegant and invaluable natural history database of the thoracic aorta, compiling information from over 3,000 patients. Between 2018 and 2019, the author had the privilege of participating in most subsequent research on the natural history of thoracic aortic disease[7]. Inspired by work from European colleagues[7], we investigated the clinical significance of ascending aortic length. Surprisingly, elongation of the ascending aorta proved to be an extraordinarily accurate predictor of adverse outcomes in ascending aortic aneurysms. Based on these findings, we proposed an ascending aortic length of 11 cm as an intervention criterion, complementing established diameter-based approaches[8]. The 2024 EACTS/STS Guidelines indicated that in patients with non-syndromic Tricuspid Aortic Valve (TAV) with "ascending phenotype", in a low-surgical-risk setting, surgery may be considered at a maximum diameter ≥ 50 mm if any of the following are present, including ascending aortic length > 11 cm[5].

Reassessment of diameter-based criteria: the aortic size paradox

The International Registry of Acute Aortic Dissection (IRAD), led by Pape *et al*., identified the so-called "aortic size paradox"[9]. This paradoxical finding revealed that a substantial proportion of aortic dissections occur in patients with aortic diameters below the conventional 5.5 cm intervention threshold[9]. This observation raised a critical question: should diameter-based aortic surgical standards be lowered?

The 2022 ACC/AHA Guideline recommended that “At centers with Multidisciplinary Aortic Teams and experienced surgeons, the threshold for surgical intervention for sporadic aortic root and ascending aortic aneurysms has been lowered from 5.5 cm to 5.0 cm in selected patients, and even lower in specific scenarios among patients with heritable thoracic aortic aneurysms[6]”. We conducted a study in 2023, encompassing three decades of experience at Yale University's Aortic Institute. It was demonstrated that 5.0 cm rather than 5.5 cm represents a more accurate intervention threshold[10]. This finding supports the concept of a "leftward shift" in surgical standards - earlier intervention based on a more profound understanding of the natural history of aortic disease.

The "phenomenon of five"

Extending the research to the descending thoracic aorta, we discovered that the probability of fatal complications (aortic rupture or death) increases sharply at two distinct inflection points: 6.0 cm and 6.5 cm. Based on these findings, setting the intervention standard at 5.5 cm appears reasonable for descending aortic aneurysms[11].

Interestingly, we observed a pattern informally termed the "Phenomenon of Five": ascending aortic aneurysms exceeding 5.0 cm are prone to dissection, descending aortic aneurysms beyond 5.0 cm are susceptible to both dissection and rupture, while abdominal aortic aneurysms larger than 5.0 cm primarily tend toward rupture. This observation provides a useful clinical mnemonic while highlighting regional differences in the natural history of aortic pathology. This phenomenon likely reflects distinct embryological origins of different aortic segments. The ascending aorta derives from neural crest cells, while the descending thoracic and abdominal segments originate from mesodermal tissue. These developmental distinctions manifest in varying extracellular matrix compositions, mechanical properties, and pathophysiological responses to hemodynamic stress.

Beyond diameter: volume assessment

The integration of multiple dimensions of aortic geometry may provide greater predictive capability than single-dimensional measurements. While a 1 mm change in aortic diameter might not attract sufficient clinical attention, it may correspond to a volume change exceeding 100 uL - representing a more readily detectable alteration in aortic geometry. Applying hemodynamic principles, we demonstrated that ascending aortic volume serves as an excellent predictor of adverse outcomes[12]. Volumetric assessment represents a promising advancement, integrating multiple aspects of aortic geometry into a single comprehensive measurement. Three-dimensional modeling reveals that volume expansion correlates more strongly with wall stress distribution than diameter alone. Advanced imaging protocols now permit semi-automated volumetric quantification with high reproducibility, facilitating clinical implementation of this metric.

Genetic considerations in surgical decision-making

Aortic genetics and phenotype are intrinsically linked. Thanks to the pioneering research by Milewicz *et al*.[13], numerous high-risk pathogenic genes associated with non-familial aortic disease have been identified. Recent advances in genetic profiling have identified specific gene mutations that dramatically alter aortic wall integrity. Variants in Fibrillin 1 (FBN1), Actin Alpha 2, Smooth Muscle (ACTA2), Transforming Growth Factor Beta Receptor 1 (TGFBR1), Transforming Growth Factor Beta Receptor 2 (TGFBR2), and Myosin Heavy Chain 11, Smooth Muscle (MYH11) genes, among others, substantially increase dissection risk even at diameters previously considered safe. It is now recommended that differentiated diameter thresholds should be based on genetic status, with earlier intervention (4.0-4.5 cm) for patients carrying high-risk mutations. The integration of genetic data into clinical algorithms represents a cornerstone of precision medicine in aortic surgery. Elefteriades provided an elegant framework for gene-based intervention criteria[14].

Bicuspid aortic valve: updated understanding

Bicuspid aortic valve (BAV) represents one of the most common cardiovascular congenital anomalies, frequently coexisting with ascending aortic dilatation. Traditional perspectives suggested aggressive management of the aorta in BAV patients with ascending aortic expansion. However, recent research challenges this assumption.

We found that the threshold for ascending aortic aneurysm surgical repair should not differ between BAV and TAV patients. Specifically, preventive surgery should be considered at 5.0 cm for both patient populations when treated at specialized centers[15]. Our recent research encompassing 698,795 individuals supports this updated understanding, demonstrating that while BAV patients exhibit higher rates of aortic enlargement (37.00%) and aneurysm formation (16.46%), the incidence of aortic dissection remains relatively low (0.74%)[16]. These findings suggest that the natural history of aortic pathology in BAV patients may be less aggressive than previously thought.

FUTURE DIRECTIONS

As our understanding of aortic disease continues to deepen, several promising avenues for further refinement of surgical standards are emerging.

Integration of multiple risk factors

Future approaches may integrate multiple risk factors - including diameter, length, volume, growth rate, family history, genetic markers, and biomechanical properties - into comprehensive risk assessment models. Machine learning algorithms may facilitate the development of personalized risk calculators that synthesize these diverse inputs to generate individualized recommendations.

Advanced imaging biomarkers

Emerging imaging technologies, including 4D flow magnetic resonance imaging (MRI) and computational fluid dynamics simulations, provide deeper insights into aortic hemodynamics and wall stress distribution. These advanced modalities may identify "vulnerable" regions of the aorta before significant abnormalities are detected by routine measurements.

Recent developments in elastography techniques permit direct assessment of aortic wall stiffness, revealing mechanical compromises that precede geometric changes[17]. Similarly, positron emission tomography using targeted radiotracers can detect inflammatory activity within the aortic wall, identifying active disease processes that may accelerate aneurysm progression[18]. The integration of these functional imaging biomarkers with traditional anatomic measurements represents a significant advancement in risk stratification.

Table 1. Evolution of surgical thresholds for ascending thoracic aortic aneurysms

Parameter	Threshold	Patient population	Evidence level	Key supporting study
Diameter-based Criteria				
Ascending aorta diameter	5.5 cm	General population (TAV)	Historical standard	Coady *et al.*, 1997[3]
Ascending aorta diameter	5.0 cm	General population (updated)	Strong	Wu *et al.*, 2023[10]
Ascending aorta diameter	5.0 cm	BAV patients	Strong	Zafar *et al.*, 2024[15]; Wu *et al.*, 2023[16]
Ascending aorta diameter	4.0-4.5 cm	High-risk genetic variants	Expert consensus	Ostberg *et al.*, 2020[14]
Body size-indexed Criteria				
Aortic cross-sectional area/height ratio	10 cm^2/m	Patients with Marfan syndrome	Moderate	Svensson *et al.*, 2002[21]
Aortic size index (ASI)	3.00 cm/m^2	General population	Moderate	Zafar *et al.*, 2018[4]
Aortic height index (AHI)	3.21 cm/m	General population	Moderate	Zafar *et al.*, 2018[4]
Length-based Criteria				
Ascending aortic length	11 cm	General population	Moderate	Wu *et al.*, 2019[8]
Volume-based Criteria				
Ascending aortic volume	197 mL	General population	Emerging	Xiao *et al.*, 2023[12]

Note: This table summarizes currently established or emerging anatomical and geometric parameters for surgical decision-making. Additional parameters not included in this table are under active investigation, including advanced imaging biomarkers (4D flow MRI for hemodynamic assessment, elastography for wall stiffness evaluation, and PET imaging for inflammatory activity), circulating molecular biomarkers (extracellular matrix proteins, inflammatory mediators, and microRNAs), and biomechanical parameters derived from computational modeling (finite element analysis). These investigational markers show promise for enhancing risk stratification but require further validation before clinical implementation. TAV: Tricuspid aortic valve; BAV: bicuspid aortic valve.

Molecular and cellular biomarkers

Circulating biomarkers reflecting aortic wall degeneration or inflammation may complement imaging-based assessments, potentially allowing earlier identification of patients at high risk for aortic complications[19]. Research in this area, including extracellular matrix proteins, inflammatory mediators, and microRNAs, shows promising results. Proteomic analysis of plasma samples from patients with progressive versus stable aneurysms has identified distinct molecular signatures that precede clinical deterioration[20]. Longitudinal biorepositories linked to clinical outcomes databases are the key for those molecular candidates advancing toward clinical implementation.

CONCLUSION

The evolution of surgical standards for ascending aortic aneurysms reflects the progressive refinement of our understanding of aortic disease. As summarized in Table 1, the field has evolved from initial crude diameter-based thresholds to current multifaceted approaches incorporating patient-specific factors, representing significant advancements in optimizing the decision-making process.

Looking ahead, the integration of anatomical, biomechanical, genetic, and molecular factors promises to further personalize surgical decision-making, ensuring that each patient receives appropriately timed intervention with optimized risk-benefit ratios. The ultimate goal remains unchanged: to intervene before catastrophic complications occur while avoiding unnecessary surgery in low-risk patients.

DECLARATIONS

Authors' contributions

The author contributed solely to the article.

Availability of data and materials

This is a perspective article based on published literature. All data referenced in this manuscript are available in the cited publications. No new datasets were generated or analyzed during the current study.

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Conflicts of interest

The author declares that there are no conflicts of interest.

Ethical approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

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