EDITORIAL
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When expansion outpaces certainty: Transcatheter Aortic Valve Replacement in patients younger than 65 years

Cuando la expansión supera la certeza: reemplazo valvular aórtico transcatéter en pacientes menores de 65 años

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Abbreviations:
TAVR = Transcatheter Aortic Valve Replacement
STS = Society of Thoracic Surgeons
ACC = American College of Cardiology
FDA = Food and Drug Administration

The contemporary evolution of Transcatheter Aortic Valve Replacement (TAVR) into progressively younger populations represents one of the most consequential shifts in structural heart disease over the past decade. In their national analysis from the STS/ACC TVT Registry, Alabbadi et al. document not merely an epidemiologic trend, but a conceptual transformation in the management of patients younger than 65 years with aortic stenosis.[1]

TAVR was originally reserved for individuals at prohibitive or extreme surgical risk. Following regulatory expansion by the U.S. Food and Drug Administration (FDA) in 2019,[2] TAVR entered the low-risk arena, supported by pivotal randomized trials such as PARTNER 3[3] and Evolut Low Risk.[4] These studies demonstrated non-inferiority, and in some cases, superiority, relative to surgery within carefully defined populations and limited follow-up horizons. Regulatory approval followed. Clinical adoption accelerated. What the present registry analysis reveals is the magnitude of that acceleration.

Between 2012 and 2024, the number of hospitals performing TAVR in patients younger than 65 years increased from 161 to 726. The median STS predicted risk of mortality declined from 3.0 to 1.8%. Most notably, the proportion of low-risk individuals in this age group increased from about 2.7 to 35.7% after the FDA approved the indication expansion in 2019.[2] Concurrently, bicuspid valve morphology (historically underrepresented in pivotal trials) approached one quarter of cases. The phenotype has shifted from highly comorbid, anatomically complex patients toward individuals with longer life expectancy and fewer conventional surgical contraindications. This change is not incremental, it is structural.

Yet the findings demand restraint in interpretation. Within the cohort younger than 65 years, an adjusted inverse

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relationship between age and one-year mortality emerged: *for every five-year increase in age, mortality decreased by approximately 10%.* In other words, the "very young" experienced higher adjusted mortality than those approaching 65. This non-linear association, absent in older age strata where mortality predictably rises with age, challenges intuitive assumptions about biological advantage. Although residual confounding and phenotypic heterogeneity may explain part of this signal, the observation remains clinically disquieting: youth alone does not confer protection in transcatheter therapy.

Equally important is the temporal limitation of available evidence. FDA approval for TAVR in low risk in August 16, 2019 was based upon trials with outcomes restricted to one year.[3,4] Structural valve degeneration, durability beyond a decade, lifetime reintervention strategies, and the biomechanical implications of bicuspid anatomy remain incompletely defined. For patients in their 50s or early 60s, a 12-month horizon represents only the prologue of a therapeutic narrative that may span in the neighborhood of three decades.

Current guidelines from the American College of Cardiology and the American Heart Association for Valvular Heart Disease continue to favor surgical aortic valve replacement in many patients younger than 65 years, largely because long-term durability data for transcatheter valves remain limited.[5] This divergence between guideline conservatism and clinical expansion reflects a familiar dynamic in cardiovascular innovation: regulatory permissibility establishes access, and practice patterns progressively redefine normality.

Approval, however, is not synonymous with equivalence across the lifespan.

The U.S. Food and Drug Administration regulates medical products, not medical judgment. Its central function in clinical medicine is to determine whether a drug or device may be legally marketed in the United States on the basis of demonstrated safety and efficacy under specified conditions. That is the extent of its mandate. Yet regulatory approval is frequently misconstrued as an endorsement of clinical supremacy. To be "FDA-approved" means that a product satisfies defined regulatory standards, is supported by sufficient evidence for commercialization, and may be used within particular indications. It does not mean that it is superior to all prior therapies, optimal for every subgroup, prudent in younger patients, or proven durable beyond the duration of studied follow-up. The FDA does not certify definitive clinical truth; it certifies conformity with regulatory thresholds. It determines whether a product may be sold. Medicine must determine whether it ought to be used. *In that distinction lies the true locus of professional responsibility.*

None of this diminishes the transformative impact of TAVR. Its procedural safety, reduced early morbidity, and rapid recovery have reshaped the therapeutic landscape of aortic stenosis. But when intervention extends into populations with extended life expectancy, durability becomes destiny. Thirty-day safety and one-year outcomes are necessary conditions for adoption; they are not sufficient conditions for generational replacement of surgery.

The expansion of TAVR into younger, lower-risk patients illustrates a broader principle: the evidentiary threshold for market entry differs from the evidentiary threshold required for lifetime therapeutic strategy. Until long-term randomized data clarify durability, valve performance in bicuspid anatomy, and optimal sequencing of reinterventions, shared decision-making must explicitly acknowledge uncertainty rather than assume resolution.

In structural heart disease, innovation defines progress.

Durability defines legacy.

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