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EDITORIAL

Cardiac Involvement in Chronic Aortic Regurgitation: Interpreting a Novel Staging Framework

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Chronic aortic regurgitation (AR) has long been approached primarily through the lens of left ventricular (LV) remodeling. LV size and systolic function, central to contemporary guideline recommendations, have shaped decision-making for decades.[1] Yet many patients with moderate to severe AR present with a wider constellation of structural and functional findings involving the left atrium, mitral valve, pulmonary vasculature, tricuspid valve, and right ventricle. These features reflect not only the hemodynamic burden of the regurgitant lesion but also age, vascular load, diastolic properties, atrial rhythm, and comorbidity profiles. In routine practice, AR is more often embedded within this broader cardiac landscape than in isolation.

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Pugliesi et al[2] extended to AR a staging concept first developed in aortic stenosis[3,4] and later adapted for primary mitral regurgitation.[5] Those earlier frameworks sought to describe cardiac involvement beyond the index valve, recognizing that multichamber abnormalities hold prognostic significance. Applying a similar construct to AR offers an opportunity to examine how an organized depiction of cardiac involvement relates to subsequent outcomes.

It is important to emphasize that the numbered stages are not intended to denote a fixed biological sequence. The abnormalities included in the framework arise from heterogeneous physiological influences, occur in varied combinations, and are not always direct consequences of AR. Rather than representing obligatory steps along a single pathophysiological continuum, the stages provide a structured summary of the extent of cardiac involvement observed at a particular point in care. This framing is central to interpreting the present study, which evaluates whether a hierarchical description of cardiac involvement offers meaningful stratification of mortality among patients managed medically.

STUDY DESIGN AND INTERPRETATION

The authors retrospectively examined more than 4000 patients with ≥moderate chronic AR across multiple Mayo Clinic sites. Cardiac involvement was grouped into five stages: no extra-valvular abnormalities (stage 0), LV involvement (stage 1), left atrium enlargement or mitral valve involvement (stage 2), pulmonary hypertension or tricuspid valve involvement (stage 3), and right ventricle dysfunction (stage 4). When multiple echocardiograms were available, the earliest study meeting the AR severity threshold was used, and each patient was assigned to the most advanced applicable stage.

Assigning patients to the highest applicable stage makes the hierarchy a cumulative index rather than a set of mutually exclusive categories. The study's own findings highlight this architecture: among patients in stages 3 and 4, most also fulfilled criteria for stages 1 and 2. This pattern is intrinsic to the classification rule

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and clarifies what the stages represent. They summarize the overall extent of cardiac involvement at presentation rather than delineating progression through discrete biological steps, and the associated gradient in mortality should, therefore, be interpreted in that context (Figure).

This distinction is particularly relevant in AR, where the components of the framework arise from multiple physiological pathways. LV remodeling plausibly reflects chronic volume load, yet downstream findings emerge through diverse mechanisms. Left atrium enlargement reflects age, blood pressure, diastolic function, and atrial rhythm. Pulmonary pressures integrate both left-sided filling conditions and intrinsic pulmonary vascular factors. Tricuspid regurgitation and right ventricular dysfunction often reflect cumulative comorbidities rather than consequences of AR alone. The staging system, therefore, captures a broad cardiac profile at the time of presentation, integrating AR severity with coexisting structural and hemodynamic features.

Within this framework, the stage-related rise in mortality reflects the cumulative nature of cardiac involvement. Over a median follow-up of 2.9 years, mortality among medically managed patients increased progressively across the hierarchy, and these associations persisted after adjustment for age, sex, AR severity, and comorbidities. Incorporating the staging construct produced a modest but statistically significant improvement in the C-statistic. Although an increment of 0.03 is small, such changes are not unusual in large observational cohorts and may still provide interpretive value by consolidating complex imaging findings into a concise summary measure.

Beyond these outcome associations, the manner in which follow-up was structured is relevant to interpretation. Outcomes were assessed only while patients remained under medical management, with censoring at aortic valve replacement, so the analysis reflects risk within the medically managed cohort. The authors report that AVR proportions were broadly similar across stages. Even with comparable rates, referral practices and assessments of operative suitability still influence which patients undergo intervention and which remain in the medical arm, considerations inherent to observational designs.

A separate interpretive consideration concerns the sex-related observations. Women appeared more frequently in advanced stages, but this may reflect differences in age, comorbidity burden, diastolic characteristics, or referral patterns rather than a specific susceptibility to AR-related cardiac damage. Without modeling designed to disentangle these factors, such findings should be regarded as descriptive.

Although the cohort spans more than a decade, the follow-up duration was relatively short. This reflects the study design, which evaluates outcomes from the qualifying echocardiogram rather than tracking transitions between stages. The framework, therefore, provides a snapshot of cardiac involvement at the time of evaluation, consistent with how staging constructs have been applied in other valve diseases.

POSITION WITHIN THE EVOLVING STAGING LITERATURE

Several principles emerge when this AR framework is placed alongside prior staging efforts. First, many patients with valve disease have structural and functional

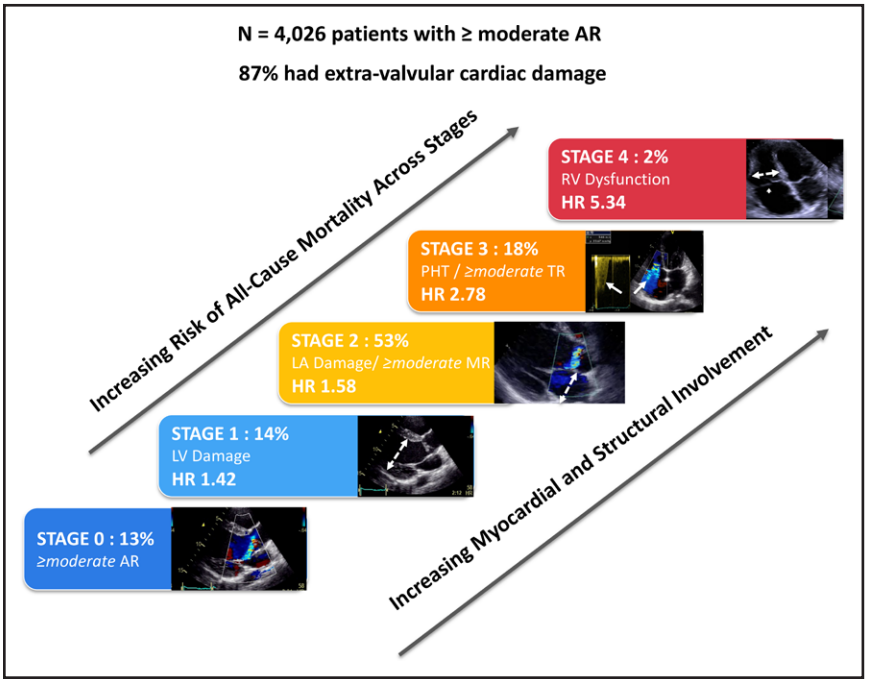

Figure. Cardiac involvement staging and prognosis in chronic aortic regurgitation (AR).
Hierarchical staging in 4026 patients with ≥moderate AR shows a progressive extension from isolated valve disease (stage 0) to left ventricle (LV) damage (stage 1), left atrial damage/mitral regurgitation (LA/MR; stage 2), pulmonary hypertension (PHT) or ≥moderate tricuspid regurgitation (TR; stage 3), and right ventricular (RV) dysfunction (stage 4). A stepwise increase in all-cause mortality is observed across stages; hazard ratios (HR) are shown relative to stage 0. Representative echocardiographic images illustrate typical findings at each stage.

abnormalities that extend beyond the index valve. A classification that captures this breadth can help clinicians appreciate the full clinical context in which AR is diagnosed.

Second, the framework is best understood as a structural descriptor rather than a biological cascade. Although numbered stages naturally suggest a sequence, the present study characterizes involvement at a single clinical assessment, not progression over time. Maintaining this conceptual clarity helps prevent overinterpretation.

Third, the findings parallel those in aortic stenosis and primary mitral regurgitation, where multi-chamber abnormalities contribute prognostic information beyond valvular severity alone. Although the incremental prognostic gain is modest, the consistency across valve diseases suggests that summarizing the broader cardiac context may refine risk assessment at the time of diagnosis.

Finally, this classification should be regarded as complementary to society-endorsed AR metrics.[6] LV size and systolic function remain central to the timing of intervention. Recognizing multichamber involvement may help identify patients who warrant closer surveillance, multidisciplinary evaluation, or more individualized management strategies.

This framework provides a structured depiction of multichamber involvement in chronic AR and underscores the broader cardiac milieu in which the disease is often encountered. Its clinical relevance will depend on longitudinal evaluation, clarification of whether transitions between stages can be observed over time, and assessment of whether integrating this information with quantitative AR parameters strengthens risk stratification or informs intervention timing. The present study lays the groundwork for such an enquiry.

ARTICLE INFORMATION

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Disclosures

None.

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