JACC
VOL. 86, NO. 4, 2025

PUBLISHED BY ELSEVIER

SPECIAL COMMUNICATION

Aortic Stenosis and Mitral Regurgitation

Takeaways From the Heart Valve Collaboratory Workshop on Multivalvular Disease

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ABSTRACT

The management of multivalvular disease presents increasing challenges in clinical practice caused by complex hemodynamic interactions and limited guideline-based recommendations. As part of the inaugural collaboration between *JACC* and the Heart Valve Collaboratory (HVC), this paper synthesizes key insights from the 2024 HVC workshop focused on concomitant aortic stenosis + mitral regurgitation. The document outlines the burden of disease, limitations of current surgical and transcatheter approaches, and variability in clinical decision-making caused by gaps in evidence. A major focus of the workshop was identifying unmet needs in patient selection, timing and sequencing of interventions, imaging, and prediction of mitral regurgitation response after transcatheter aortic valve replacement. The paper highlights unresolved clinical questions and proposes a research agenda including the establishment of prospective registries, randomized trials comparing staged vs concomitant therapy, and use of artificial intelligence for imaging analysis and risk prediction. By bringing together multidisciplinary expertise and outlining priorities for future investigation, this initiative seeks to advance the standardization and personalization of multivalvular disease management. These efforts aim to improve outcomes for patients with complex valve disease and serve as a framework for addressing other multivalve combinations in future research. (JACC. 2025;86:271-279) © 2025 by the American College of Cardiology Foundation.

The management of multivalvular disease (MVD) has emerged as one of the most complex challenges in contemporary cardiovascular care, driven by an aging population with increasing prevalence of degenerative valve pathologies and expanded therapeutic options.[1,2] Current guidelines from major societies provide limited guidance on managing concomitant valve disease, particularly regarding optimal timing, sequencing, and patient selection for interventions. This knowledge gap has led to significant variability in clinical practice and underscores the urgent need for evidence-based consensus. The Heart Valve Collaboratory (HVC) workshop on MVD, held in November 2024, focused on specific valve combinations (day 1 addressed aortic and mitral valve [MV] disease; day 2 focused on tricuspid and left-sided valve disease) to address these challenges. This rapid communication summarizes key insights from the workshop on concomitant aortic stenosis (AS) and mitral regurgitation (MR), emphasizing current knowledge, clinical challenges, and a forward-looking research agenda. A forthcoming comprehensive document will address the various combinations, including tricuspid valve

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The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

Manuscript received April 21, 2025; revised manuscript received May 12, 2025, accepted May 21, 2025.

ISSN 0735-1097/$36.00
https://doi.org/10.1016/j.jacc.2025.05.053

ABBREVIATIONS AND ACRONYMS

AS = aortic stenosis

AVR = aortic valve replacement

MR = mitral regurgitation

MV = mitral valve

MVR = mitral valve replacement

MVr = mitral valve repair

MVD = multivalvular disease

SAVR = surgical aortic valve replacement

TAVR = transcatheter aortic valve replacement

TEER = transcatheter edge-to-edge repair

involvement and management of futile "Cohort C" patients. Figure 1 provides a visual synthesis of the burden of disease, management decisions, research agenda, and key knowledge gaps addressed throughout this report (Figure 1).

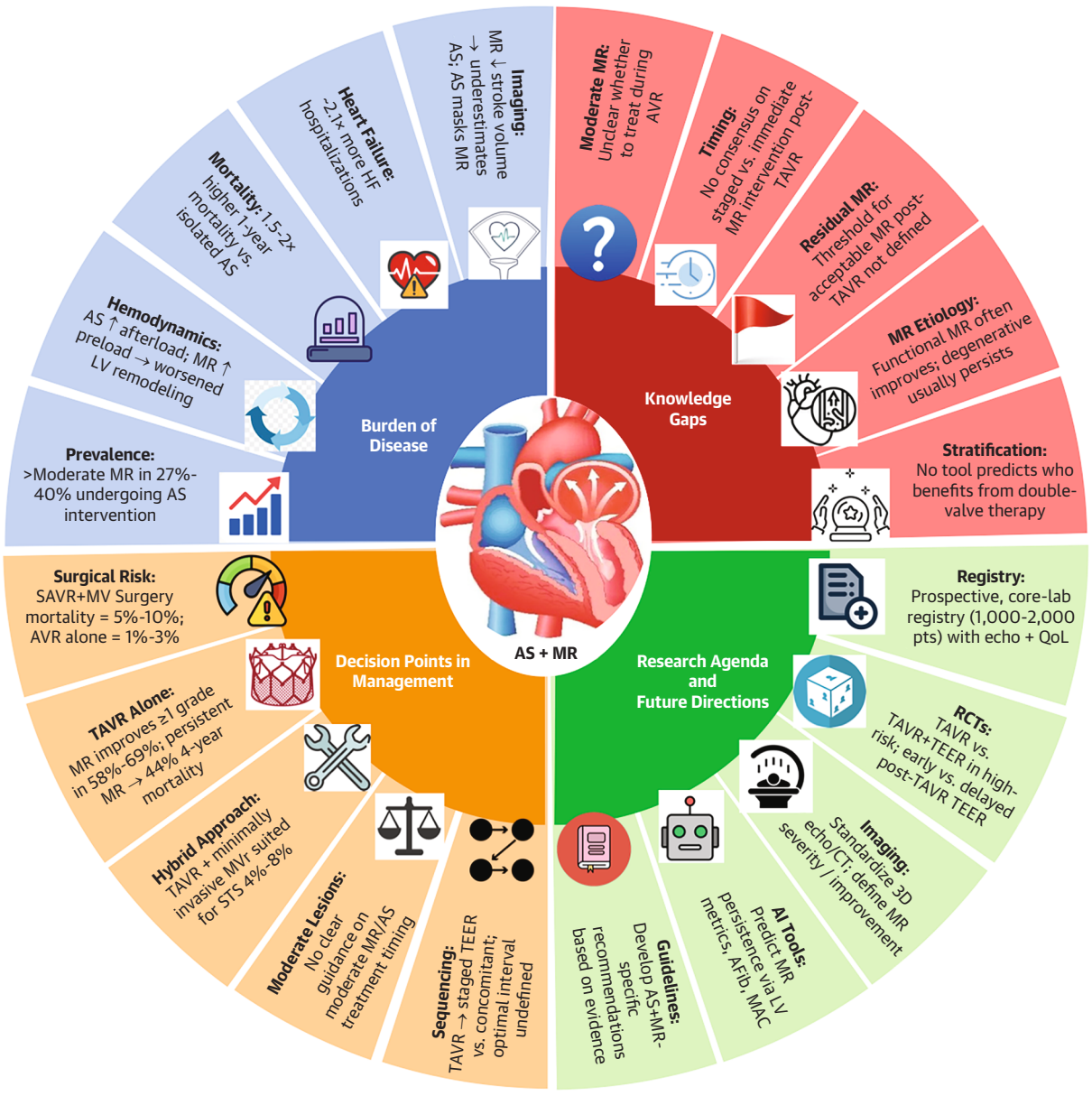
AS WITH MR (AS+MR)

EPIDEMIOLOGY AND CLINICAL BURDEN. Concomitant AS+MR is the most common left-sided multivalve combination, observed in roughly one-quarter to one-third of patients with severe AS.[3,4] Contemporary registries report moderate-or-severe MR in about 27% to 40% of patients undergoing intervention for severe AS, making this multivalve disease combination a frequent clinical scenario.[3,4] When significant AS and MR coexist, their hemodynamic effects compound one another, leading to an amplified burden on the heart. AS-induced pressure overload can exacerbate MR severity (afterload mismatch), while MR's volume overload worsens the diastolic dysfunction of AS, together accelerating left ventricular (LV) remodeling and failure. In addition, this combination of hemodynamic abnormalities may complicate the diagnosis of individual valvular disease severity. Consistently, patients with severe AS+MR experience worse outcomes than those with isolated AS. Observational studies have shown approximately 1.5- to 2-fold higher mortality at 1 year for severe AS with ≥ moderate MR compared with isolated AS.[5,6] They also have higher rates of heart failure hospitalization (eg, ~2.1 times greater risk) and markedly worse quality of life (KCCQ health status scores ~15-20 points lower) in the year following diagnosis. These data underscore the substantial clinical burden of AS+MR, justifying aggressive efforts to optimize management strategies in this high-risk population. These key aspects of clinical burden and management complexity are summarized in Table 1.

SURGICAL MANAGEMENT AND OUTCOMES. For patients at low surgical risk, the traditional gold-standard treatment for severe AS+MR has been double-valve surgery—ie, surgical aortic valve replacement (SAVR) combined with either mitral valve repair (MVr) or replacement (MVR) in the same operation. Surgery offers the advantage of definitive correction of both lesions, and for patients with long life expectancy and reparable primary MR, a surgical approach is often favored. However, combined aortic valve replacement (AVR) + MV surgery carries significantly higher perioperative risk than isolated valve surgery. Contemporary data from large U.S. inpatient samples show an in-hospital mortality of ~5% to 6% for SAVR+MV repair and ~8% to 10% for SAVR+MV replacement, compared with ~1% to 3% for isolated AVR.[7,8] In other words, operative mortality is 2 to 3 times higher with a double-valve procedure, reflecting the added complexity and patient comorbidity burden. Important predictors of surgical outcome include the etiology of MR and the patient's ventricular function.[9,10] Patients with primary (degenerative) MR derive survival benefit from mitral repair over replacement (5-year survival ~78% vs 62% in secondary MR, if repaired).[10] Those with severely reduced LV ejection fraction (<30%) or other comorbidities face a substantially elevated operative risk (eg, a 3-fold mortality increase for LV ejection fraction <30%).[9] The presence of mitral annular calcification can also complicate mitral surgery, sometimes necessitating replacement over repair.[11] In a small single-site study, double valve surgery conveyed no survival benefit compared with transcatheter aortic valve replacement (TAVR) alone.[12] Indeed, regression of MR may occur in 50% to 70% of patients following isolated SAVR and 50% of patients undergoing isolated TAVR.[13] Despite these challenges, surgical AVR+MV intervention can be lifesaving and durably effective in appropriately selected patients. Guidelines recommend double valve surgery for severe AS and severe primary MR unless patients are high or prohibitive surgical risk, when staged transcatheter procedures could be considered.[14] For severe AS and severe secondary MR, the data is less convincing for double surgery and for these patients shared decision-making about double surgical or staged transcatheter therapies are appropriate.

Although current surgical guidelines generally recommend intervening on a second valve if the lesion is severe, but recommendations for moderate secondary lesions are less clear[15] with recent American College of Cardiology/American Heart Association guidelines removing the indication to intervene for moderate MR at the time of AVR for lack of evidence.[14] In fact, studies suggest that survival for double surgery if concomitant MR is severe or isolated AVR if MR is moderate, and is better than isolated AVR if MR is severe.[13] A recent meta-analysis of 13 nonrandomized studies suggested the moderate or less FMR without predictors of deterioration should be treated conservatively with isolated AVR, while moderate-severe functional MR, particularly with predictors of deterioration such as atrial fibrillation, enlarged left atrium, high LV mass index, pulmonary hypertension, or lower peak transaortic gradients,

FIGURE 1 Navigating the Complexity of Concomitant AS+MR



AFib = atrial fibrillation; AI = artificial intelligence; AS = aortic stenosis; AVR = aortic valve replacement; CT = computed tomography; HF = heart failure; LV = left ventricle; MAC = mitral annular calcification; MR = mitral regurgitation; MV = mitral valve; QoL = quality of life; RCT = randomized controlled trial; RV = right ventricle; SAVR = surgical aortic valve replacement; STS = Society of Thoracic Surgeons; TAVR = transcatheter aortic valve replacement; TEER = transcatheter edge-to-edge repair.

may benefit from double valve surgery.[16] In those patients with moderate AS and severe MR, recommendations are lacking. One single-site study suggested that 5-year survival free from severe AS was higher in the SAVR replacement group; however, there was no significant difference in all-cause mortality.[17] Finally, the ability to use transcatheter solutions to treat MR may change the threshold for

TABLE 1 Current Clinical Burden and Management Challenges in Concomitant AS and MR

Issue	Why It Matters
High prevalence	AS+MR is the most common left-sided valve combination, seen in ~27%-40% of patients referred for TAVR; rates increase with age and comorbidity.
Increased mortality	Concomitant AS+MR is associated with ~1.5× to 2× higher 1-y mortality than isolated AS, particularly when MR persists after intervention.
Persistent MR post-TAVR	Moderate-or-greater MR persists in ~30%-50% of patients following TAVR, leading to ongoing symptoms and poor long-term outcomes.
Functional impairment	AS+MR patients experience lower health status and QoL, with ~2.1× greater risk of HF hospitalizations compared with isolated AS.
Complex hemodynamics	Combined pressure and volume overload alters LV remodeling, complicates diagnosis, and confounds grading of AS or MR severity.
Diagnostic limitations	MR reduces stroke volume, often masking true AS severity; conversely, AS-driven gradients can obscure MR significance.
Predicting MR response	There are no reliable predictors for MR improvement after TAVR, particularly in mixed or functional MR etiologies.
Surgical risk amplification	Double-valve surgery carries 2× to 3× operative mortality compared with isolated valve procedures; benefits must outweigh added procedural risk.
Transcatheter complexity	AS+MR often requires staged transcatheter intervention caused by anatomical constraints, procedural risk, or reimbursement challenges.
Patient frailty and comorbidities	Severe MAC, RV dysfunction, PH, and frailty limit candidacy for surgical or transcatheter options, creating therapeutic inertia.
Imaging standardization gaps	Lack of consensus on how to quantify AS+MR using echo/CT contributes to variability in diagnosis, referral, and trial eligibility.

AS = aortic stenosis; CT = computed tomography; HF = heart failure; LV = left ventricle; MAC = mitral annular calcification; MR = mitral regurgitation; PH = pulmonary hypertension; QoL = quality of life; RV = right ventricle; TAVR = transcatheter aortic valve replacement.

double valve surgery. The workshop highlighted the need for better evidence to guide these decisions, as practice varies widely.

TRANSCATHETER MANAGEMENT AND OUTCOMES. The advent of TAVR over the past decade has transformed the treatment landscape for AS, enabling minimally invasive therapy even in high-risk and older patients. For patients with AS+MR who are poor surgical candidates (eg, high Society of Thoracic Surgeons risk scores or frailty), a transcatheter strategy is often considered. Treating the aortic stenosis first with TAVR can sometimes alleviate secondary MR because of unloading of the left ventricle. Indeed, significant MR improves in an estimated 30% to 60% of patients after TAVR, especially when the MR is secondary (functional) in nature.[18] For example, one registry noted MR severity decreased by ≥1 grade at 30 days in ~58% to 69% of patients post-TAVR.[19] However, this leaves a substantial subset with persistent MR. Studies have shown that moderate-or-worse MR persists after TAVR in roughly 30% to 50% of cases.[19] The prognosis for these patients is concerning—persistent significant MR post-TAVR is associated with *higher mortality* and rehospitalization compared with those in whom MR regresses. In 1 multicenter analysis, 4-year mortality was ~44% in patients with post-TAVR MR ≥ moderate vs ~32% to 35% in those whose MR improved or was mild.[20] The low-flow, low-gradient severe AS population similarly shows an improvement in MR in ~44%, with persistence of MR >2+ an independent predictor of the primary outcome of 1-year death or heart failure hospitalization.[18,21] Key predictors of MR improvement after TAVR include MR etiology and anatomical factors: patients with functional MR (caused by LV dilation) and favorable anatomy (eg, no severe mitral annular calcification, smaller vena contracta) are more likely to see MR reduction, whereas those with primary MR, heavy annular calcification, atrial fibrillation, or very large left atria often have MR that *persists* despite TAVR.[19]

These observations raise critical questions: Which AS+MR patients can be managed with TAVR alone, and who should receive concomitant or staged mitral intervention? The workshop emphasized that there is no one-size-fits-all answer; careful case-by-case evaluation by a heart team is essential, incorporating surgical risk, MR mechanism, and patient goals.

For patients with severe AS+MR who remain high-risk or inoperable, transcatheter mitral therapies have become an important adjunct to TAVR. The 2 main approaches are a staged strategy—performing TAVR first, then assessing MR and potentially treating it in a second procedure—vs a concomitant transcatheter strategy, treating both valves in the same setting. The staged approach (TAVR → reassess → transcatheter edge-to-edge repair [TEER] later) is currently more common, allowing time to see if MR improves and to plan the mitral intervention if needed. However, staging prolongs the overall treatment course and leaves patients exposed to interim heart failure risk if MR is severe. A concomitant approach (eg, TAVR immediately followed by TEER in the same procedure) is appealing to achieve complete therapy in one session, although it requires significant expertise and carries procedural

complexity. Early experiences with combined TAVR+TEER have demonstrated high technical success rates (on the order of 85%-95% for achieving successful implants in both valves).[22,23] Small series suggest that performing TAVR and TEER together is feasible with acceptable early outcomes—for instance, 30-day mortality around 4% to 7% in high-risk patients, which appears comparable to or even slightly better than doing the procedures separately in sequence.[22,23] It should be noted, however, that patients selected for concomitant therapy are highly specific, and no randomized data exist yet to prove an outcome advantage. Thus, whether to treat severe AS+MR with TAVR alone, TAVR plus a planned staged mitral intervention, or a simultaneous double transcatheter approach remains an individualized decision. The workshop panel highlighted the need for more data on optimal sequencing: eg, if staging, what is the ideal interval to wait post-TAVR before intervening on MR, and if doing concomitant TEER, what patient/anatomic factors predict success or failure of this combined approach?

KEY MANAGEMENT CHALLENGES AND UNRESOLVED QUESTIONS. Managing AS+MR requires navigating several unique challenges. First, accurate assessment of disease severity can be difficult—severe MR can cause a low forward stroke volume, potentially underestimating AS gradients, while AS can mask the true impact of MR.[24] Advanced imaging techniques (integrated echocardiography, computed tomography, magnetic resonance imaging) are often needed to characterize each lesion's severity and the interplay between them. Standardizing how we quantify AS severity in the presence of MR (and vice versa) is a priority, because misclassification can lead to suboptimal treatment decisions. Second, heart failure management in dual-valve disease is complex: clinicians must balance afterload reduction (to relieve AS pressure load) with preload optimization (to manage MR), all while avoiding hypotension or pulmonary edema. Patients with severe AS+MR are prone to acute decompensation, and in advanced cases may require temporary mechanical circulatory support or even consideration of transplant/LV assist device if both valve lesions cannot be corrected in time. Another challenge is determining the timing of intervention for each lesion. Uncertainty persists about scenarios such as: *severe AS with moderate MR*—should the MR be surgically or percutaneously addressed at the time of AVR/TAVR, or can one defer and only treat AS initially? Conversely, *moderate AS with severe MR*—should one proceed with mitral surgery/TEER and hold off on the AS until it progresses further, or is upfront double intervention warranted? The workshop discussions revealed a lack of consensus, reflecting the scant evidence available. Additionally, when both AS and MR are severe, deciding between a single-stage (surgery or transcatheter) vs a 2-stage approach is challenging, and factors like MR etiology (primary vs secondary), patient age, and institutional expertise all influence the strategy.

Key unresolved questions identified include:

- **Patient Selection:** Which patients truly benefit from adding a mitral intervention to AS treatment? For example, can TAVR alone suffice in an elderly patient with secondary MR that might improve, or will they do better with TEER as well? Conversely, in a relatively young patient with primary MR, is it ever acceptable to do TAVR and TEER instead of surgery, or would that sacrifice long-term durability?
- **Optimal Sequencing:** If a combined transcatheter approach is chosen, is it better to perform the mitral repair immediately after TAVR or to stage it days/weeks later? Does treating AS first always make subsequent mitral repair safer, or could delaying leave the patient at risk of interim heart failure? No trials have answered this.
- **Imaging and Monitoring:** How should we follow patients after treating one valve to decide if the second valve now warrants intervention? What degree of residual MR post-TAVR is acceptable, and for how long, before pulling the trigger on a second procedure? Advanced echocardiographic criteria to guide this need definition.
- **MR Etiology Influence:** Does the cause of MR (degenerative leaflet disease vs functional caused by LV dysfunction) change the calculus in AS+MR management? Intuitively yes—degenerative MR often will not resolve without intervention—but specific thresholds for intervention in each scenario are not well defined by data

The most pressing unanswered questions in AS+MR management are outlined in Table 2. Addressing these questions will require targeted research efforts, as discussed in the following text.

RESEARCH AGENDA FOR AS+MR

The HVC workshop strongly endorsed the development of dedicated research initiatives to improve the evidence base for AS+MR management. A summary of proposed scientific initiatives and strategic priorities is provided in Table 3. Key components of the

TABLE 2 Unresolved Knowledge Gaps in the Management of Concomitant AS and MR

Gap	Why It Matters
Timing and sequencing	No randomized data guide whether MR should be addressed during the index TAVR or in a staged manner; timing may impact MR regression and outcomes.
Imaging predictors	No validated imaging-based model predicts which MR will improve post-TAVR, complicating procedural planning and patient selection.
Device strategy	Optimal device choice (eg, edge-to-edge repair, annuloplasty, chordal platforms) for MR in AS+MR context remains undefined, especially post-TAVR/SAVR.
Atrial vs ventricular MR	AFMR and VFMR behave differently following AS relief, but clinical trials often do not stratify patients by mechanism, limiting personalized treatment.
Right-sided sequelae	Persistent MR contributes to pulmonary hypertension and tricuspid regurgitation; long-term data on these downstream effects are limited.
Moderate lesions	Limited consensus on whether to intervene on moderate MR during AVR or moderate AS during MV surgery; impact on progression and outcomes remains unclear.
Residual MR tolerance	No clear threshold defines acceptable residual MR post-TAVR; moderate MR after intervention is associated with worse outcomes in observational studies.
MR etiology and prognosis	MR mechanism (functional vs degenerative) influences likelihood of improvement post-TAVR, but is not routinely incorporated into risk models.
Risk stratification tools	No validated tool exists to identify which AS+MR patients benefit most from double-valve intervention vs single-valve approach.
Futility and advanced care	Futility thresholds for patients with severe comorbidities (eg, MAC, RV dysfunction) are poorly defined; guidance on palliative or investigational care is lacking.

AFMR = atrial functional mitral regurgitation; SAVR = surgical aortic valve replacement; VFMR = ventricular functional mitral regurgitation; other abbreviations as in Table 1.

research agenda include prospective registries and randomized trials:

- **Multicenter Registry:** Establish a large prospective registry of patients with AS+MR to understand natural history and treatment outcomes. A registry enrolling on the order of 1,000 to 2,000 patients across centers would allow detailed subgroup analyses (eg, severe AS + moderate MR, moderate AS + severe MR, and severe AS + severe MR subsets). Core data elements would include standardized echocardiographic measurements (with core laboratory review to ensure uniformity), assessments of MR mechanism (primary vs secondary), quantification of mitral annular calcification, and longitudinal tracking of outcomes and quality of life. Such a registry could answer fundamental questions like: What is the natural history of untreated moderate MR in patients who undergo SAVR or TAVR for AS? Conversely, what happens to moderate AS if one intervenes on MR alone? What patient factors predict MR improvement after TAVR and long-term survival with TAVR alone? And how do real-world outcomes compare between different management strategies (medical therapy vs TAVR vs surgery vs combination)? These data would inform hypothesis generation and trial design.
- **Randomized Trials:** Several trial concepts were proposed to directly compare management strategies:

1. **TAVR Alone vs TAVR+M-TEER:** In high-surgical-risk patients with *severe AS + severe secondary MR*, a randomized trial could compare TAVR alone vs TAVR with concomitant TEER in the same procedure. The primary endpoint might be a 1-year composite of death or heart failure hospitalization, testing whether upfront dual-valve therapy improves outcomes or merely adds risk and cost. This trial would clarify the benefit of addressing MR at the time of TAVR in those who cannot undergo surgery.
2. **Optimal Timing of Staged Therapy:** For patients with *severe AS + severe MR* who undergo TAVR first, a trial could randomize to an early planned TEER at, eg, 1 month post-TAVR vs a deferred strategy (watchful waiting with option for TEER at 6 to 12 months if MR remains significant). Key outcome measures would include degree of MR reduction, LV remodeling, and clinical outcomes at 1 year. This would inform whether an early second intervention is beneficial or if many patients improve and avoid it.
3. **Surgery vs Hybrid Approach:** In intermediate-risk patients (Society of Thoracic Surgeons ~4%-8%) who are candidates for both approaches, a trial could compare conventional open double-valve surgery (AVR + MV repair) vs a hybrid approach of TAVR followed by a minimally invasive surgical or transcatheter mitral repair. Endpoints at 1 to 2 years could include survival free of reintervention, recovery times,

TABLE 3 Scientific Priorities and Strategic Recommendations for Advancing the Management of Concomitant AS and MR

Initiative/Recommendation	Why It Matters
Registry development	Prospective, international AS+MR registries with core laboratory adjudication, MR mechanism classification, and QoL tracking are essential for real-world insights.
Targeted randomized trials	Trials comparing TAVR alone vs TAVR+M-TEER (high-risk), early vs delayed MR repair (persistent MR), and surgery vs hybrid approach (intermediate-risk) will guide care.
Standardized imaging protocols	Multimodal imaging (echo, CT, CMR) with unified severity grading enables better diagnosis, follow-up, and inclusion criteria for trials.
AI-driven predictive tools	Machine learning models can forecast MR persistence post-TAVR and support decision-making around double-valve therapy.
MR mechanism-based stratification	Functional and degenerative MR differ in pathophysiology and response to AS relief, but are often lumped together in trials, limiting precision care.
"Cohort C" patients	Defining futility thresholds and creating personalized pathways for frail, high-risk patients expands appropriate access and avoids over-treatment.
Access to investigational therapies	Advanced disease patients need expanded eligibility for transcatheter and medical therapies beyond standard surgical options.
Guideline integration	Data from AS+MR studies should inform broader MVD guideline updates, including tricuspid involvement and end-stage heart failure ("Cohort C") populations.
Personalized clinical pathways	Risk-adapted, algorithmic approaches based on anatomy, MR etiology, and procedural sequencing are essential for optimizing patient outcomes.

AI = artificial intelligence; CMR = cardiac magnetic resonance; MVD = multivalvular disease; other abbreviations as in Table 1.

and quality of life. As transcatheter options expand, this would clarify if outcomes approach surgical results in this risk cohort, potentially expanding options for patients who wish to avoid open surgery.

- **Advanced Imaging and Analytics:** The research agenda also highlights the need for innovation in imaging and data analysis. Standardized multimodality imaging protocols should be developed for AS+MR—eg, combining 3-dimensional echocardiography and cardiac computed tomography to better predict which MR will improve after TAVR. Trials and registries should incorporate core laboratory analysis to minimize variability in MR grading. Additionally, applying artificial intelligence and machine learning to imaging and clinical data could help identify patterns (eg, a predictive model for MR persistence post-TAVR based on valve morphology and ventricular metrics). Such tools might eventually guide personalized decision-making (eg, an AI risk score to decide between TAVR alone vs TAVR+TEER).

Collectively, these studies and innovations would fill the evidence gaps in AS+MR, providing clarity on optimal management that today is lacking. The Heart Valve Collaboratory aims to facilitate many of these efforts by coordinating among institutions and aligning stakeholders on research priorities.

RECOMMENDATIONS AND CALL TO ACTION

From the workshop's deliberations, several clear recommendations emerged to improve care for patients with AS+MR:

- ***Immediate Priorities:*** Form an international AS+MR registry with standardized data collection and imaging review to begin accruing evidence. In parallel, convene an expert panel (heart teams, imagers, surgeons) to develop consensus definitions for assessing AS+MR severity (eg, how to grade AS when MR is present, uniform criteria for "MR improvement" postintervention). This will ensure that future studies speak the same language and that clinicians have interim guidance while awaiting trial results.
- ***Midterm Goals:*** Launch the proposed randomized trials to compare treatment strategies, because these will provide the highest level of evidence for guidelines. Also, invest in validating emerging technology—such as AI algorithms for predicting outcomes or automating imaging analysis—to support clinical decision-making in multivalve cases.

- ***Long-Term Vision:*** Integrate the findings from registries and trials into updated valvular heart disease guidelines that specifically address concomitant AS+MR. Ultimately, extend the collaborative framework developed for AS+MR to other common valve combinations (eg, AS with tricuspid regurgitation, or MR with tricuspid regurgitation), as well as to the challenging "Cohort C" patients who are not candidates for any conventional treatment. The goal is a future where management of MVD is evidence-based, standardized, and personalized to each patient's unique profile.

CONCLUSIONS

The 2024 HVC workshop underscored that aortic stenosis with concomitant mitral regurgitation is a pressing clinical problem that exemplifies the broader challenges of MVD. Patients with AS+MR face high morbidity and mortality, and current approaches to their management are hampered by limited data. By convening experts and outlining a focused research agenda, the HVC has taken a crucial first step toward closing this gap. A coordinated strategy of collaborative research, guideline development, and innovation is urgently needed to improve outcomes in AS+MR. The insights gained will not only benefit this sizeable patient population but also serve as a template for tackling other complex valve combinations. Through ongoing collaboration and investigation, the cardiovascular community aims to deliver more personalized, evidence-based care for all patients with multiple valve disease, moving us closer to optimal outcomes even when "aortic stenosis is not alone."

FUNDING SUPPORT AND AUTHOR DISCLOSURES

Dr Hahn has received speaker fees from Abbott Structural, BaylisMedical, Edwards Lifesciences, Medtronic, and Philips Healthcare; and has institutional consulting contracts for which she receives no direct compensation with Abbott Structural, Boston Scientific, Edwards Lifesciences, Medtronic, and Novartis. Dr Ailawadi has served as a consultant for Medtronic, Edwards, Abbott, Gore, Anteris, AtriCure, Cryolife, Johnson and Johnson, Philips, and Jena. Dr Tang has received speaker honoraria and served as a physician proctor, consultant, advisory board member, TAVR publications committee member, RESTORE study steering committee member, APOLLO trial screening committee member, and IMPACT MR steering committee member for Medtronic; has received speaker honoraria and served as a physician proctor, consultant, advisory board member and TRILUMINATE trial anatomic eligibility and publications committee member for Abbott Structural Heart; has served as an advisory board member for Boston Scientific; has served as a consultant and physician screening committee member for Shockwave Medical; has served as a consultant for Philips and Edwards Lifesciences, Peija Medical, and Shenqi Medical Technology; and has received speaker honoraria from Siemens Healthineers. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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REFERENCES

1. Falk V, Baumgartner H, Bax JJ, et al. 2017 ESC/EACTS guidelines for the management of valvular heart disease. *Eur J Cardiothorac Surg*. 2017;52(4):616–664.

2. Iung B, Baron G, Tornos P, Gohlke-Bärwolf C, Butchart EG, Vahanian A. Valvular heart disease in the community: a European experience. *Curr Probl Cardiol*. 2007;32(11):609–661.

3. Bedogni F, Latib A, De Marco F, et al. Interplay between mitral regurgitation and transcatheter aortic valve replacement with the CoreValve Revalving System: a multicenter registry. *Circulation*. 2013;128(19):2145–2153.

4. Mavromatis K, Thourani VH, Stebbins A, et al. Transcatheter aortic valve replacement in patients with aortic stenosis and mitral regurgitation. *Ann Thorac Surg*. 2017;104(6):1977–1985.

5. Sannino A, Losi MA, Schiattarella GG, et al. Meta-analysis of mortality outcomes and mitral regurgitation evolution in 4,839 patients having transcatheter aortic valve implantation for severe aortic stenosis. *Am J Cardiol*. 2014;114(6):875–882.

6. Nombela-Franco L, Eltchaninoff H, Zahn R, et al. Clinical impact and evolution of mitral regurgitation following transcatheter aortic valve replacement: a meta-analysis. *Heart*. 2015;101(17):1395–1405.

7. Vassileva CM, Li S, Thourani VH, et al. Outcome characteristics of multiple-valve surgery: comparison with single-valve procedures. *Innovations (Phila)*. 2014;9(1):27–32.

8. Arshad HB, Minhas AMK, Khan SU, et al. National trends and outcomes of surgical aortic valve replacement with concomitant mitral valve surgery. *Cardiovasc Revasc Med*. 2022;40:13–19.

9. Vollenbroich R, Stortecky S, Praz F, et al. The impact of functional vs degenerative mitral regurgitation on clinical outcomes among patients undergoing transcatheter aortic valve implantation. *Am Heart J*. 2017;184:71–80.

10. David TE, Armstrong S, McCrindle BW, Manlhiot C. Late outcomes of mitral valve repair for mitral regurgitation due to degenerative disease. *Circulation*. 2013;127(14):1485–1492.

11. Alexis SL, Malik AH, El-Eshmawi A, et al. Surgical and transcatheter mitral valve replacement in mitral annular calcification: a systematic review. *J Am Heart Assoc*. 2021;10(7):e018514.

12. Yu P-J, Mattia A, Cassiere HA, et al. Should high risk patients with concomitant severe aortic stenosis and mitral valve disease undergo double valve surgery in the TAVR era? *J Cardiothorac Surg*. 2017;12(1):123.

13. Zilberszac R, Gleiss A, Binder T, et al. Prognostic relevance of mitral and tricuspid regurgitation in patients with severe aortic stenosis. *Eur Heart J Cardiovasc Imaging*. 2018;19(9):985–992.

14. Otto CM, Nishimura RA, Bonow RO, et al. 2020 ACC/AHA guideline for the management of patients with valvular heart disease: executive summary: a report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *J Am Coll Cardiol*. 2021;77(4):450–500.

15. Nishimura RA, Otto CM, Bonow RO, et al. 2017 AHA/ACC focused update of the 2014 AHA/ACC guideline for the management of patients with

valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *J Am Coll Cardiol*. 2017;70(2):252–289.

16. Kowalówka AR, Onyszczuk M, Wańha W, Deja MA. Do we have to operate on moderate functional mitral regurgitation during aortic valve replacement for aortic stenosis? *Interact Cardiovasc Thorac Surg*. 2016;23(5):806–809.

17. Weingarten N, Rekhtman D, Iyengar A, Song C, Patel M, Atluri P. Aortic valve replacement for moderate aortic stenosis during mitral surgery improves survival free from severe stenosis. *Asian Cardiovasc Thorac Ann*. 2023;31(6):475–482.

18. Ferruzzi GJ, Silverio A, Giordano A, et al. Prognostic impact of mitral regurgitation before and after transcatheter aortic valve replacement in patients with severe low-flow, low-gradient aortic stenosis. *J Am Heart Assoc*. 2023;12(17):eO29553.

19. Tzikas A, Piazza N, van Dalen BM, et al. Changes in mitral regurgitation after transcatheter aortic valve implantation. *Catheter Cardiovasc Interv*. 2010;75(1):43–49.

20. Witberg G, Codner P, Landes U, et al. Effect of transcatheter aortic valve replacement on concomitant mitral regurgitation and its impact on mortality. *JACC Cardiovasc Interv*. 2021;14(11):1181–1192.

21. Freitas-Ferraz AB, Lerakis S, Barbosa Ribeiro H, et al. Mitral regurgitation in low-flow, low-gradient aortic stenosis patients undergoing TAVR: insights from the TOPAS-TAVI registry. *JACC Cardiovasc Interv*. 2020;13(5):567–579.

22. Elbadawi A, Elgendy IY, Afify H, et al. Combined transcatheter aortic and mitral valve interventions: insights from a national database. *JACC Cardiovasc Interv*. 2021;14(13):1505–1507.

23. Zubarevich A, Zhigalov K, Szczechowicz M, et al. Simultaneous transaortic transcatheter aortic valve implantation and off-pump coronary artery bypass: an effective hybrid approach. *J Card Surg*. 2021;36(4):1226–1231.

24. De Zan G, van der Bilt IAC, Broekhuizen LN, et al. Non-invasive assessment of multivalvular heart disease: a comprehensive review. *Rev Cardiovasc Med*. 2024;25(1):29.

KEY WORDS aortic stenosis, double-valve intervention, mitral regurgitation, mitral valve repair, multivalvular disease, surgical aortic valve replacement, transcatheter aortic valve replacement, transcatheter edge-to-edge repair