STATE-OF-THE-ART REVIEW

Artificial Intelligence in Valvular Heart Disease



Innovations and Future Directions

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ABSTRACT

Managing valvular heart disease (VHD) requires integrating multimodal data, including demographics, symptoms, biomarkers, electrocardiogram findings, and imaging studies. However, the capacity and processing power of the human mind are limited, particularly in the current era where vast quantities of complex data require rapid processing. Integrating artificial intelligence (AI) into the management of VHD offers an opportunity to enhance diagnostic accuracy, streamline clinical workflows, optimize procedural strategies, and predict outcomes and disease progression. Subsets of AI such as machine learning and deep learning algorithms can uncover the unseen data from routine investigations (eg, electrocardiograms, echocardiography, and computed tomography), providing robust and accurate risk prediction tools to inform personalized treatment strategies. Intraprocedurally, AI-based enhancements in imaging guidance can be leveraged to improve procedural safety and success. Digital twin technology can allow case-specific disease modelling, such as simulating valve designs and predicting adverse events, fostering precision medicine. By using the full potential of AI, clinicians can provide a comprehensive, personalized management strategy for VHD patients, ultimately enhancing clinical outcomes. However, models based on AI algorithms require rigorous validation across multiple centers to ensure their reliability. Concerns about bias, data privacy, and limited transparency challenge the application of AI decision-making to digital health care. This review discusses the applications of AI in the management of patients with VHD, highlights the future directions of AI technologies, and considers the challenges of integrating AI into clinical practice. (JACC Cardiovasc Interv. 2025;18:2439-2457) © 2025 by the American College of Cardiology Foundation.

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ABBREVIATIONS AND ACRONYMS

AI = artificial intelligence

AUROC = area under the receiver-operating characteristic curve

CT = computed tomography

DL = deep learning

ECG = electrocardiogram

LLM = large language models

LVOT = left ventricular outflow tract

ML = machine learning

TAVR = transcatheter aortic valve replacement

VHD = valvular heart disease

he management of valvular heart disease (VHD) involves the assimilation of heterogeneous information, ranging from structured data in electronic health records (eg, demographics, symptoms, and laboratory values) to unstructured data from electrocardiograms (ECGs) and imaging. As the volume and complexity of data increases, it becomes harder for human cognitive capabilities to process and analyze these data effectively. Artificial intelligence (AI) enables computers to mimic human cognitive function at magnitudes beyond human capacity.

Through machine learning (ML) and deep learning (DL) (Figure 1) integrating AI into the management of VHD can enhance diag-

nostic accuracy, predict disease progression, streamline clinical workflows, and optimize procedural strategies (Central Illustration). In addition, various ML techniques, for example, supervised learning and unsupervised clustering, have been applied to predict outcomes after valve intervention.¹

Importantly, despite the potential of AI, models based on ML or DL must undergo rigorous validation across diverse patient cohorts, from multiple centers, before being applied clinically. Prospective validation is essential to ensure their reliability, akin to how clinical trials are required to establish the safety and efficacy of novel therapeutic interventions.

This review discusses the applications of AI in the management of VHD, highlights the future directions of AI technologies, and considers the challenges of integrating AI into clinical practice.

AI-AUGMENTED DIAGNOSIS AND SEVERITY ASSESSMENT OF VHD

VHD is underdiagnosed, with many patients being identified at advanced disease stages. Auscultation is a low-cost, first-line diagnostic tool, hence the application of well-validated ML algorithms to optimize auscultation for early diagnosis of VHD is

HIGHLIGHTS

- Managing VHD involves the assimilation of a large volume of heterogenous multimodal data, making it difficult for human cognitive capabilities to effectively process and analyze.
- Integrating AI in the management of VHD enables clinicians to provide robust personalized management strategies, enhances diagnostic accuracy and decision-making, streamlines clinical workflows, optimizes procedural success, and improves the accuracy of outcome prediction.
- Models based on AI algorithms require rigorous validation in multicenter studies to ensure their reliability. Further challenges for the transition to digital health care include concerns about potential bias, data privacy, and limited transparency in AI decision-making.

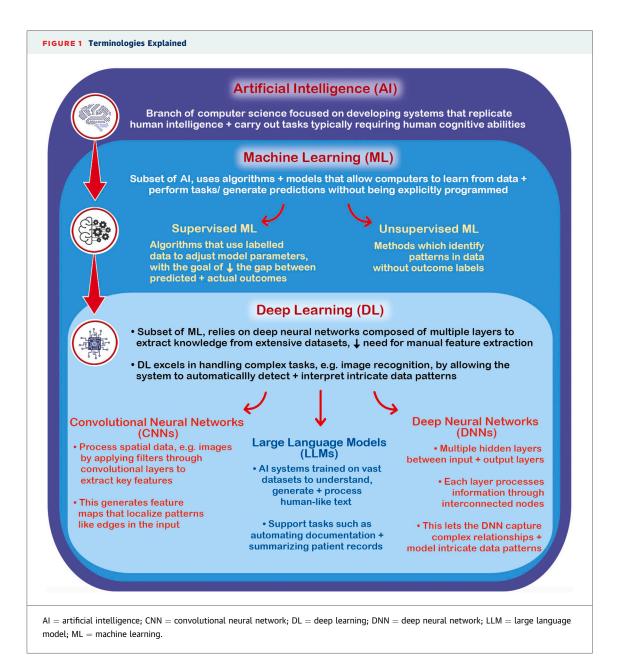
worth pursuing. The ECG is another attractive modality for AI-augmented screening of VHD, due to its widespread availability, low-cost, and standardized digital format. Echocardiography is the main modality for evaluating VHD, but is more time-consuming, requires skilled imagers and acquisition errors lead to measurement variability, therefore AI optimized echocardiography is of interest. Ultimately, the ideal approach would be a multimodal AI and ML framework that integrates data from various AI-based models (auscultation, ECG, echocardiography, computed tomography [CT], cardiac magnetic resonance imaging) to assist in diagnosis, risk prediction and treatment of VHD.^{2,3}

AUSCULTATION. Auscultation skills have diminished in recent decades. Compared with echocardiography, auscultation has low sensitivity for detecting VHD, especially aortic regurgitation and mild or moderate valve disease. 5,6 Digitized acoustic

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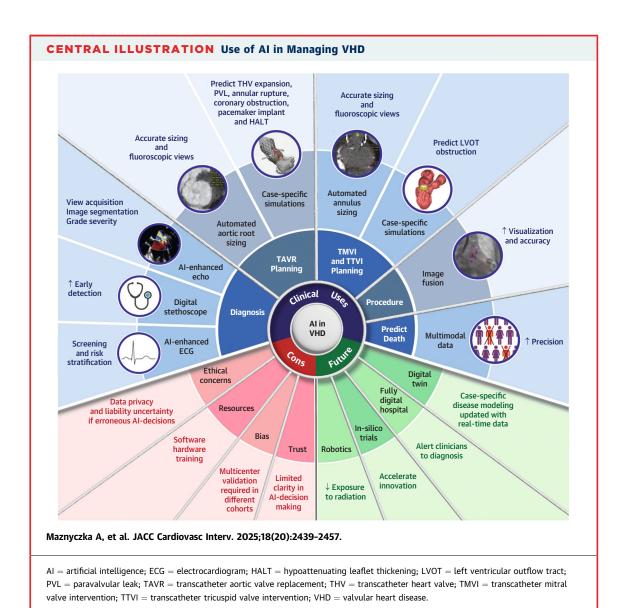
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data can be processed for use by DL algorithms to produce output that can guide the physician toward the correct interpretation. Several AI-enabled digital stethoscopes have been developed and marketed, and are being evaluated for diagnostic accuracy.^{7,8} For detecting aortic stenosis, the VoqX AI-enhanced stethoscope system (Sanolla) achieved high diagnostic accuracy (sensitivity 84%, specificity 92%).⁷ By contrast, the Eko murmur analysis software performed considerably worse for detecting VHD (sensitivity 39%, specificity 82%).⁸ Before adopting

AI algorithms for auscultatory enhancement, they should be trained on large datasets and meticulously validated. One such validation study encouragingly detected pathologic murmurs with 86% sensitivity and 84% specificity.⁹

ELECTROCARDIOGRAM. Recent studies have demonstrated progress in applying convolutional neural networks, a type of DL, to ECG data for VHD detection.¹⁰ The ValveNet model was developed and validated across multiple sites with over 77,000 patients



and achieved a sensitivity of 78% and specificity of 73% (area under the receiver-operating characteristic curve [AUROC] of 0.84) for detecting ≥moderate aortic stenosis, aortic regurgitation, or mitral regurgitation. The model performed better for aortic stenosis than for mitral or aortic regurgitation (AUROCs: 0.88, 0.83, and 0.77, respectively). Similar results were observed in an analysis from the Mayo Clinic of 258,607 adults, with performance improving when incorporating age and sex data (AUROC: 0.87). 12

Beyond improving early detection of VHD, AI-enhanced ECG analysis may predict the progression of structural heart disease, enabling more precise risk stratification. As an example, the PRESENT-SHD (practical screening using ensemble ML strategy for structural heart disease) model, validated across multiple cohorts, showed that individuals with positive AI-ECG screens had 2 to 4 times higher risk of developing new-onset structural heart disease or heart failure. Successful clinical adoption of AI-guided ECG screening will depend on thorough validation across diverse health care settings, seamless integration into existing clinical workflows, and clear demonstration of improved patient outcomes.

ECHOCARDIOGRAM. The main applications of AI in echocardiography are: image/view acquisition15; image segmentation of anatomical structures for automated analysis¹⁶; detection of significant VHD,^{17,18} identification of high-risk phenogroups, 19,20 and live fusion with fluoroscopy. Importantly, AI may improve the detection of VHD in health care settings without access to trained sonographers, indeed with AI guidance, the percentage of evaluable images acquired by novice nurses performing echocardiograms was 92%, 96%, and 83% for the aortic, mitral, and tricuspid valves, respectively.21 Commercial AI companies have developed the ability to accurately identify severe aortic stenosis from echocardiograms without left ventricular outflow tract (LVOT) data.²² For detecting high-severity aortic stenosis, a ML model (trained on echocardiograms from 1,052 patients) demonstrated 99% accuracy when compared with experienced echocardiographers.²³ For quantification of mitral regurgitation, a novel DL system, which intakes a complete transthoracic echocardiogram, identifies color Doppler videos, and determines mitral regurgitation severity on a 4-step ordinal scale using the reading cardiologist as a reference standard, has shown slightly more accurate classification of mitral regurgitation using multiple transthoracic echocardiography views compared with only apical 4-chamber views (82% vs 80%). 17 AI algorithms can also correctly grade the severity of aortic regurgitation and tricuspid regurgitation,18 for example, an AI automation pipeline, EchoNet-TR, identified cases of ≥moderate tricuspid regurgitation with an AUROC >0.93 and a negative predictive value >0.89, with strong grading concordance with cardiac magnetic resonance imaging.²⁴

AI-enhanced echocardiography can also predict the progression of aortic^{3,25} and mitral¹⁸ regurgitation, with the potential to aid decision-making on the timing of intervention, and can stratify patients according to risk of periprocedural adverse events²⁰ and mortality.^{1,19,26,27} Of note, when high-quality images are used in the training data, the algorithm can lead to errors in analysis when applied to suboptimal imaging, which can occur in real-world practice. The solution is ongoing training of algorithms with real-world data to ensure the detection and exclusion of suboptimal echocardiographic imaging and errors in echocardiographic measurements.

COMPUTED TOMOGRAPHY. AI can quantify aortic and mitral valve calcification from non-gated chest CT scans, thereby enabling opportunistic detection of VHD.²⁸ Furthermore, DL models provide automated aortic valve calcium quantification using contrast-

enhanced CT and show excellent agreement with Agatston scores derived from noncontrast CT scans, ²⁹ thereby facilitating the assessment of aortic stenosis severity when echocardiographic findings are equivocal.

MORTALITY PREDICTION GUIDED BY AI

AI has emerged as a powerful tool for risk stratification and mortality prediction in VHD.30 Unlike the traditional risk scores, AI-based approaches incorporate a broader set of longitudinal and multimodal data (including multiple imaging modalities²), offering a more comprehensive assessment of procedural risk and disease progression.³¹ In patients where clinical ambiguity persists, such as those with low-flow, low-gradient aortic stenosis, echocardiographybased ML algorithms can integrate global longitudinal strain (a marker of early subclinical myocardial dysfunction) and left ventricular remodeling metrics for a more refined risk stratification.32 ML models using cardiac magnetic resonance or CT imaging have also been shown to predict prognosis in aortic stenosis.33,34 By incorporating frailty markers (eg, sarcopenia, gait speed, and nutritional status) and postprocedural factors (eg, paravalvular leak severity and left ventricular remodeling), these AI-based mortality predictions may be further refined.^{34,35} For predicting mortality after mitral-TEER, AI-derived risk scores (EuroSMR, 36 MitrAI, 37 and MITRALITY 38), which integrate clinical, procedural, and echocardiographic parameters, outperformed conventional models. Overall, AI-driven models have the potential to offer superior risk stratification by integrating multimodal datasets, although potential biases, methodological transparency, and reproducibility remain concerns.

AI FOR PLANNING TRANSCATHETER AORTIC VALVE REPLACEMENT

The success of transcatheter aortic valve replacement (TAVR) relies on precise preprocedural CT assessment of the aortic root and vascular anatomy to determine patient eligibility, prosthesis sizing, and access strategy. To address the increasing demand for efficient CT analysis, ^{39,40} advanced semi-automated and fully automated methods have been developed, which use DL algorithms to automatically segment cardiac structures, followed by anatomical landmark detection and aortic root identification. A summary of commercial AI companies and technologies is provided in Supplemental Table 1.

3mensio Structural Heart (Pie Medical) is a widely used semiautomated TAVR planning tool, offering 2and 3-dimensional (3D) assessments of the aortic root. However, key measurements for TAVR sizing, and risk stratification remain a manual, timeconsuming process prone to observer variability. Fully automated software packages such as 4TAVR (Hi-D Imaging) and HeartNavigator (Philips Healthcare) automatically provide essential measurements for TAVR planning.³⁹ Exploratory data indicate that these packages provide fast, accurate segmentation and measurements. However, validation studies have excluded certain anatomical variants (eg, bicuspid morphology) limiting system robustness. To address this gap and meet practical needs, the FOR-SSMANN algorithm has recently been developed and validated as a fully automated tool capable of detecting and classifying valve phenotypes (bicuspid, severely calcified, etc) and anatomical risk factors (eg, horizontal aorta and calcification distribution) with high consistency and reliability.⁴⁰

Although the aforementioned tools provide precise aortic root anatomy for geometric transcatheter heart valve sizing, they do not account for the mechanical interaction between the TAVR and surrounding tissues. Patient-specific simulation technologies such as FEops HEARTguide (FEops-Materialise) and DASI Simulations, validated against post-TAVR CT scans, incorporate the geometric and mechanical properties of both the transcatheter valve and host anatomy (Figure 2). FEops HEARTguide integrates finite element technology to predict TAVR frame expansion, apposition, and contact pressure on host tissue. Studies have demonstrated its ability to predict calcium displacement, frame deformation, conduction abnormalities, and paravalvular leak in patients undergoing TAVR. 41-43

DASI Simulations use physics-based AI and reducer-order modeling to simulate TAVR deformation within patient-specific native anatomy. The resulting outputs are combined with ML algorithms to generate computationally derived quantitative biomarkers that help assess the risk of various postprocedural complications, for example, coronary obstruction, annular rupture, and hypoattenuating leaflet thickening. The accuracy of AI models for predicting hypoattenuating leaflet thickening may be increased by incorporating clinical features, for example, platelet/coagulation biomarkers and post-TAVR echocardiographic and CT features (such as valve underexpansion). DASI simulations also incorporate pre-TAVR echocardiographic data with CT imaging to predict post-TAVR transvalvular gradivalve leaflet shear stress, and

dynamics.^{44,45} Randomized clinical trials are underway to evaluate how patient-specific simulation may add value over standard CT planning in real-world clinical practice.⁴⁶

TAVR planning for younger patients must address the challenges of future TAVR-in-TAVR procedures and the risk of pacemaker implantation. ML models that integrate CT with clinical, ECG and echocardiographic data can robustly predict pacemaker impost-TAVR.47 For TAVR-in-TAVR procedures, the upward displacement of the old valve leaflets by the new valve frame creates a neoskirt that may impair coronary access and flow. Additionally, the risk of patient-prosthesis mismatch increases as multiple stented frame layers accumulate within the annulus, progressively reducing the residual valve area. FEops HEARTguide and DASI Simulations allows for the virtual implantation of sequential TAVRs, accounting for the mechanical and physical properties of the valve-in-valve construction and its interaction with adjacent tissue. 48 This approach offers insights into coronary accessibility and residual effective orifice areas and may guide TAVR type, size, and implantation target depth for both index and sequential TAVR procedures (Figure 3).

AI FOR PLANNING OF TRANSCATHETER MITRAL AND TRICUSPID VALVE INTERVENTIONS

AI is already used relatively routinely for planning transcatheter mitral and tricuspid valve interventions, particularly for valve replacements (Figures 4, 5, and 6). ML allows automated identification and measurement of the mitral and tricuspid annulus within seconds. 49 Patients evaluated for transcatheter mitral valve replacement tend to have challenging anatomies, for example, mitral annular calcification, or anatomies at risk for LVOT obstruction, therefore selecting eligible patients can be timeconsuming. During transcatheter mitral valve replacement, the anterior mitral valve leaflet is displaced toward the LVOT, creating a confined neo-LVOT area, and AI models for CT analysis can predict the risk of LVOT obstruction.⁵⁰ This planning process involves annular segmentation, mitral valve trajectory, neo-LVOT centerline generation, and planimetric quantification of neo-LVOT size using a simulated valve frame. A similar method can be applied to 3D echocardiographic datasets with high concordance with CT analyses.⁵¹ Most simulations assume uniform valve expansion, failing to account for patient-specific anatomical variations and the dynamic tissue-stent interactions during Rupture

FIGURE 2 Examples of TAVR Planning and Patient-Specific Simulations Showing Prediction of HALT, Paravalvular Leak, and Aortic Root Simulations for Predicting TAVR Complications A HALT New case CT scan **3D Visual Model HALT Analysis** ML SPEED model model Clinical experience **B** Paravalvular Leak Predicted gap sizes accounting for alterations in balloon filling volume **BEV 29 BEV 29 Nominal** +1cc +2cc Gap sizes: 2.9 + 2.2mm | 2.6 + 2.1mm 3.1 + 2.8mm Arrow heads show predicted flow trajectories of leak Left-right cusp Non-coronary cusp C Aortic Root Rupture Stretch **BEV 26 Nominal** BEV 26 - 1cc BEV 26 - 2cc Visual hotspots showing stretch experienced by the aorta as the volume in the balloon expandable valve (BEV) is altered

Schematic outline of the DASI simulation workflow, where a transcatheter aortic valve replacement (TAVR) computed tomography (CT) scan is used to create a 3-dimensional (3D) virtual model, and then a simplified force-driven particle model (SPEED) is generated where machine learning (ML) algorithms can: (A) assess the risk of subsequent hypoattenuating leaflet thickening (HALT); (B) predict the risk of paravalvular leak; and (C) predict the risk of aortic root rupture after TAVR using a computationally derived biomarker that detects the amount of stretch experienced by the aorta with balloon-expandable valve (BEV) deployment. The software can account for varying implant depths and alterations in balloon filling volume. In C, the surface area of the visual hot spots dynamically changes as the volume of the balloon is modulated.

deployment. DASI Simulation's SPEED (simplified force-driven particle model) technology can be applied to CT simulations of transcatheter mitral valve replacement to predict how the transcatheter valve frame will deform in a patient's anatomy, and can illustrate the impact of procedural modifications, such as LAMPOON (laceration of the anterior mitral valve leaflet to prevent LVOT obstruction) (Supplemental Figure 1).

At present, computational simulations for mitral transcatheter edge-to-edge repair remain largely exploratory. Previous studies have leveraged CT data to evaluate how different transcatheter edge-to-edge repair device placements affect relevant parameters including mitral annular dimensions, regurgitant orifice area, and transvalvular gradient. ^{52,53} However, CT imaging is not routinely performed for transcatheter edge-to-edge repair planning. A scalable methodology capable of predicting hemodynamic outcomes using only routine preprocedural patient-specific information is essential for broader clinical adoption.

As a next step, companies are developing and validating full cardiac-cycle CT-analysis software, which can generate patient-specific simulations of transcatheter mitral or tricuspid valve implantations and even mitral transcatheter edge-to-edge repair procedures.

MITRAL AND TRICUSPID VALVE INTERVENTIONS FACILITATED BY AI

The cornerstone of applying AI advances to clinical practice is to achieve procedural simplification (eg, automating tasks and standardizing workflows), and to make outcomes more reproducible. Indeed, integration of AI into cardiac structural intervention procedures has demonstrated improved procedural efficiency and consistency.⁵⁴ A particularly useful AI innovation is intraprocedural image fusion, which harnesses real-time data to support complex mitral and tricuspid valve procedures (Figure 6). Advanced tools such as EchoNavigator (Philips Healthcare) employ AI to generate 3D heart models based on the detection of cardiac structures on transesophageal echocardiography, complete with precise segmentation of anatomical structures such as cardiac chambers, and valvular annuli.55 Once the segmentation of the 3D volume dataset is performed, the software must "coregister" the shape of the transesophageal echocardiography probe with the fluoroscopic tilt (caudal or cranial) and rotational angle to fuse both modalities. This allows the fused real-time echocardiographic image to change its orientation on the fluoroscopic image, based on both the location of the probe and the C-arm position, enabling dynamic intraprocedural visualization of patient anatomy. Echo-fluoro fusion improves communication between the imager and interventionalist by allowing the 2 different imaging perspectives to be visualized on a single screen. This fusion imaging system is available with the latest-generation transesophageal echocardiogram probes and is also expected to be developed for intracardiac echocardiography in the near future.

Integrating echo-CT and fluoro-CT fusion technologies can enhance intraprocedural guidance 56,57 and may enhance procedural accuracy in some situations. By combining 3D transesophageal echocardiography or fluoroscopy with preprocedural CT imaging, fusion imaging enables precise positioning of the transcatheter mitral or tricuspid valve replacement at the annular plane, may contribute to a faster and more efficient assessment of coaxiality, and could simplify a paravalvular leak closure procedure. A limitation of fused CT images is that these are static and can be subject to coregistration inaccuracies.

As mitral and tricuspid valve interventions become increasingly complex and widely adopted, AI-driven technologies may offer superior visualization and real-time navigation. The challenge for the imager is to continuously image the device throughout the procedure while showing the interventionalist the correct orientation and position of the desired target, especially during mitral transcatheter edge-to-edge repair. A novel software DeviceGuide (EchoNavigator SmartVue, Philips) facilitates this process by using AI to continuously identify both the mitral transcatheter edge-to-edge repair device and 3D transesophageal echocardiography probe face on fluoroscopic imaging. By recognizing the 3D transesophageal echocardiography probe face, the location of the 3D volume dataset can be identified on the fluoroscopic image. While the imager maintains the device within the 3D volume dataset, DeviceGuide automatically reforms the 3D volume into multiplanar reconstructed 2dimensional images without operator interaction. Different DeviceGuide models can: 1) simultaneously display onto the multiplanar images, device trajectory, position, and orientation relative to the target; and 2) continuously track the device to maintain a stable image despite respiratory motion or probe manipulation (Figure 7). This novel AI software could reduce errors in interpretation of device trajectory, position, and orientation, thereby improving the accuracy of device implantation, shorten procedure times by reducing the need for frequent multi-planar readjustment of imaging, and reduce complications by continuously imaging the device movement relative to the adjacent structures.

EDUCATION AND TRAINING SIMULATIONS USING AI

The application of AI in simulation-based training for VHD is in its early stages. Most AI advancements have focused on precision medicine, decision support, and procedural planning rather than hands-on training. AI enables more realistic simulation environments, which can allow physicians to overcome steep learning curves of low-frequency, high-complexity procedures (Figure 8).⁵⁸ Notably, AI can improve understanding of 3D cardiac navigation by visualizing the relationship between different anatomical structures, and can create algorithms for step-bystep valve intervention guidance. Furthermore, extended virtual, augmented, and mixed reality is an emerging medical imaging display platform (Figure 8),59 which enhances training and guides complex procedures.

Another promising approach is the analysis of user behavior during simulations. By examining how different individuals manipulate and deploy medical devices, AI can identify patterns, detect common errors, and provide targeted feedback. Additionally, an AI-driven "proctor" could offer real-time guidance tailored to the trainee's skill level, adjusting the difficulty and support dynamically, which, once proven reliable, could guide real-life procedures. Moreover, generative AI techniques are used to create life-like fluoroscopy and ultrasound images, making training simulations more realistic. 60

Looking toward the future, AI models could learn from real-world procedural data to refine device behavior simulations, making virtual training even more representative of actual clinical conditions. Although these applications are still under development, AI-driven training solutions could significantly improve procedural competency.

AI BEYOND THE VALVE FOR VHD

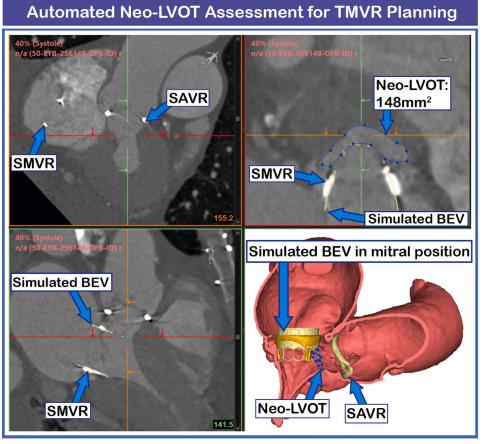
Most AI studies in VHD have centered on the direct assessment of valves; however, the potential of AI goes far beyond the valve itself. Disease progression leads to extravalvular cardiac damage, including remodeling of the atria and ventricles, myocardial dysfunction, and hemodynamic alterations that affect the pulmonary and renal circulations. Cardiac magnetic resonance and CT imaging can play a

FIGURE 3 Patient-Specific Simulation of a TAVR-in-TAVR Procedure Based on a Preindex TAVR CT Scan Simulation of Coronary Access/ Obstruction for a Future **TAVR-in-TAVR Procedure** Predicts: Valve-to-coronary distance Valve-to-STJ distance Neo-skirt height simulated at node 4 of a SEV Colormap scale: Colormap Red colour = 2mm* reflects gap <2mm distance between top of the 4mm neo-skirt and aortic root Values above this maximum are displayed in the highest color in the scale Multiple simulations at various implantation depths of the **BEV** relative BEV at node 6 to the SEV BEV at node 5 BEV at node 4

Analysis and images generated by means of FEops HEARTguide (FEops-Materialise). The patient was scheduled for a first TAVR; this patient-specific simulation aimed to assess the feasibility of a future TAVR-in-TAVR procedure, assessing the risk of coronary obstruction and/or inaccessibility. CRP = coronary risk plane (base of the lowest patent coronary ostia); NSP = neoskirt plane (top of the neoskirt); SEV = self-expanding valve; STJ = sinotubular junction; other abbreviations as in Figure 2.

crucial role in myocardial characterization by quantifying extracellular volume expansion, which aids in the diagnosis and prognosis of amyloidosis and other cardiomyopathies superimposed on VHD.⁶¹ These imaging modalities provide detailed tissue characterization, helping to identify early myocardial changes that may influence treatment decisions. Integrating AI algorithms enhances the accuracy and efficiency of analyzing myocardial extracellular volume on CT and magnetic resonance imaging, improving risk stratification and outcome prediction.

FIGURE 4 Example of an Automated Neo-LVOT Assessment for TMVIV Planning, to Assess the Risk of LVOT Obstruction in a Patient With a Prior Surgical Mitral Valve Bioprosthesis

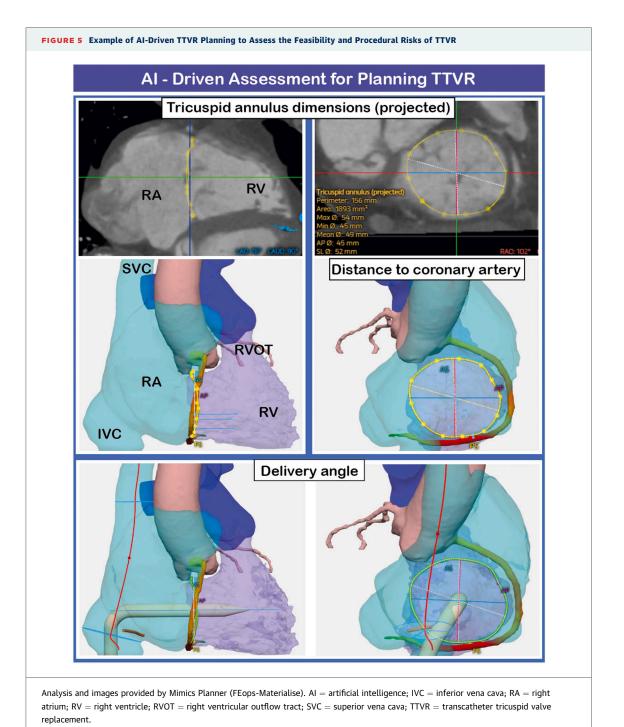


Analysis and images generated by means of Mimics (FEops-Materialise). BEV = balloon expandable valve; LVOT = left ventricular outflow tract; SAVR = surgical aortic valve replacement; SMVR = surgical mitral valve replacement; TMVIV = transcatheter mitral valve-in-valve.

This approach may be particularly valuable for patient with moderate VHD, allowing early intervention to prevent irreversible cardiac damage and improve long-term outcomes. Additionally, patient-specific factors including genetics, age, body composition, and other comorbidities add another layer of complexity, making a personalized and integrative approach essential for optimal VHD management.

AI holds promise in addressing these complexities by enabling comprehensive, automated analysis across multiple datasets and modalities. AI-driven segmentation and quantification of imaging datasets enable detailed anatomical and functional assessments, which extend from valves to cardiac structures (automated volumetric analysis of cardiac chambers, ejection fraction, strain) and the vascular system. Furthermore, AI-based body composition analysis in CT and magnetic resonance imaging can quantify fat, muscle, bone, and other organ composition to identify novel biomarkers for risk stratification, thereby capturing metabolic and structural factors that influence the outcomes of VHD patients. 62

AI-driven approaches offer opportunities to analyze largescale databases that integrate valvular and cardiovascular structural data with genomic information through imaging-genomics methodologies. This approach can help uncover genetic determinants of VHD pathophysiology for personalized treatment strategies. By using the full potential of AI, clinicians can move beyond a valve-centric approach toward a comprehensive, patient-centered management strategy, ultimately enhancing therapeutic decision-making, risk prediction, and outcomes.

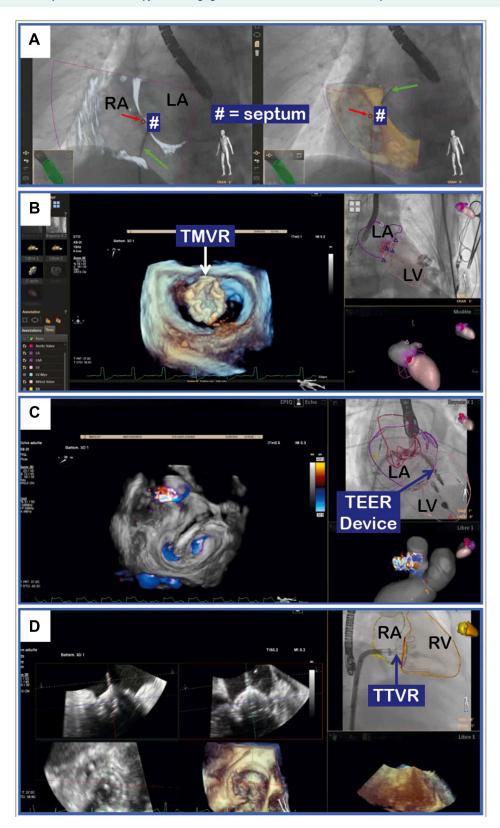


FUTURE DIRECTIONS

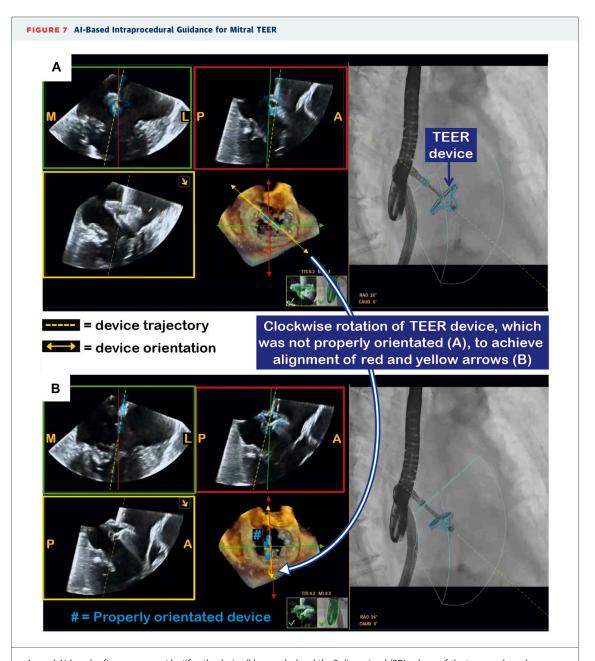
The adoption of AI technology accelerates the transition to digital health care. A future is foreseeable whereby the diagnosis and severity assessment of VHD and preprocedure planning will become fully automated. In a fully digital hospital, the use of natural language processing to extract diagnosis,

symptoms, and demographic and clinical data from the electronic health record could be combined with AI-driven analysis of data from digital stethoscopes, ECGs, and echocardiography to provide a fully integrated system to alert clinicians to diagnosis and progression of VHD. In addition to the hospital setting, the widespread adoption of wearable technology offers the opportunity for continuous

FIGURE 6 Examples of Echo-Fluoroscopy Fusion Imaging to Guide Transcatheter Mitral and Tricuspid Interventions



(A) Two and 3-dimensional transesophageal echocardiography combined with marker superimposition during transeptal puncture. (B) Left cardiac chambers overlay during TMVR using a transapical approach. (C) Left cardiac chambers overlay during mitral-TEER in a patient with temporary left ventricular assist. (D) Right cardiac chambers overlay during TTVR using a transfemoral approach. Images in B to D are generated by means of the Heart Model, Philips. LA = left atrium; LV = left ventricle; TEER = transcatheter edge-to-edge repair; TMVR = transcatheter mitral valve replacement; other abbreviations as in Figure 5.



A novel Al-based software program identifies the device (blue overlay) and the 3-dimensional (3D) volume of the transesophageal echocardiography probe, allowing for automated generation of multiplanar images for intraprocedural guidance of mitral TEER. The medial (M)-lateral (L) (green box) and posterior (P)-anterior (A) (red box) multiplanar images are automatically generated by DeviceGuide for continuous information about device position as well as trajectory (yellow dashed lines) in these planes. The yellow box (which replaces the standard "blue box") continuously shows an on-axis image of the device. The 3D en face view shows the target (intersection of the green and red lines), as well as the orientation of the device (yellow line). In this example, the initial device orientation in the left atrium (A) requires the paddles be clockwise rotated, to align with the target red line (B). When the device is aligned with the red target line, the images in the red box and yellow box should be the same. In this example, the trajectory will require further adjustment to align with the green and red lines on the 2D images. Abbreviations as in Figures 5 and 6.

FIGURE 8 Example of an AI-Based Simulation and Intraprocedural Guidance Α AI - Enhanced Simulators Al-enhanced image **Unenhanced image** LCC RCC NCC :::: mentice **Augmented Reality CEP Guidance** В a

(A) Al-enhanced fluoroscopic imaging for TAVR on images provided by Mentice AB. (B) Virtual reality visualization and manipulation of a virtual 3D model of the patient's aortic arch (A) and a virtual copy of live fluoroscopy (B) in augmented reality while placing cerebral embolic protection (CEP) filters under fluoroscopy (C). Reproduced with permission from Sadri et al.⁵⁹ LCC = left coronary cusp; NCC = noncoronary cusp; RCC = right coronary cusp; other abbreviations in Figures 5, 6, and 7.

AI-facilitated ambulatory monitoring of VHD patients beyond traditional clinical environments; for example, identifying the risk of deterioration in those with known severe aortic stenosis awaiting TAVR, or monitoring for conduction disturbances postprocedure to enable safe early discharge.⁶⁴

It is envisaged that digital twin technology (virtual replicas of physical systems continuously updated with real-time or periodic data) will offer casespecific disease modelling,65,66 as has already been demonstrated in cardiac electrophysiology procedures. Digital twin technology can allow clinicians to virtually test different valve types before interventions, simulate various scenarios, and select the best approach. Conventional simulations (often mislabeled as digital twins) lack adaptability, whereas a true digital twin integrates pre- and posttreatment data, continuously refining itself over time. 65,66 For a digital twin in VHD to be effective, it must go beyond static simulations and allow continuous, bidirectional interaction between the physical (patients) and digital counterparts, using real-time sensor integration. Dynamically updating digital twins with data from wearable devices (eg, continuous ECG monitors), implantable pressure sensors in prosthetic valves, and serial follow-ups enables dynamic adaptation and provides feedback for clinical decision-making (eg, identification of valve deterioration). 65,66 Of note, AI-driven analysis combined with computational fluid dynamics could help predict adverse events, such as valve thrombosis by assessing abnormal flow patterns, shear stress, and patient-specific hemodynamic changes, allowing for early intervention and personalized treatment adjustments.

During valve interventions, it is anticipated that advances in assisted and virtual reality will guide the operator in real-time, whereas robotics could reduce the need for in-room medical staff.⁶⁷ Notably, a remotely controlled robotic system for transesophageal echocardiography has already demonstrated reliable, fast, and accurate performance in preclinical tests and could reduce radiation exposure to the imager.⁶⁸ During valve deployment in TAVR, AI models can analyze invasive pressure tracings to detect early signs of valve malposition or hemodynamic instability, enabling immediate correction. During transcatheter edge-to-edge repair, AI can provide real-time anatomical tracking for enhanced procedural navigation, helping operators to precisely position the clip to maximize leaflet capture and reduce regurgitation. Moreover, with the advent of large language models (LLM), interactive copilots facilitate physician-device interaction for optimal transducer placement in echocardiography. The concept of cognitive interventional suites will further support interventionalists in their routine by automatically detecting the phase of the procedure, by analyzing key patterns of the workflow and predicting the remaining procedure time, or by providing automatic context information from the electronic health record at the right time of the procedure.

We will see a major step towards improving the realism of cardiac simulators by generative AI techniques. These methods could generate different scenarios for the trainee from a LLM input. The LLM could further instruct the trainee of the next procedural step or provide context information on its inherent difficulties. Finally, the development of insilico clinical trials can potentially accelerate novel valve device development, by replacing animal studies and human trials with virtual models to evaluate device performance⁶⁹; however, the virtual representation of the physical system needs to be proven to be credible.

LIMITATIONS OF AI

Despite the potential of novel AI approaches, there are limitations (Central Illustration). Although AI is generally superior to standard methods for estimating quantitative parameters from medical images, ML models for risk prediction might not outperform traditional models,70 especially for rare events, or when informed by a limited number of clinical variables or a small number of patients. Furthermore, AI models developed using data that are not representative of the target population may be biased and have a detrimental impact on realworld clinical applications.71 Ensuring that derivation, validation, and external datasets for AI models accurately represent the underlying patient populations is crucial to minimizing bias in the resulting algorithms. Of note, inputting the raw data rather than report data from investigations, for example, ECG, echocardiography, or CT, is crucial for AI to learn from the data and generate the output. To confirm that the output is correct, it needs to be validated by a core laboratory or an expert reader. At present, this approach is not standardized. Future studies must focus on inputting raw data and validating output with a core laboratory, to promote quality and accuracy. Importantly, comparing different algorithms on the same dataset is being used to validate and improve each algorithm and to minimize errors. 72,73 This approach can identify the best algorithms for the dataset and can improve the results by changing algorithm parameters. Managing

missing data and outliers is a particularly challenging aspect, which might lead to errors in data interpretation, and common approaches are to either delete patients with missing/outlier values from the analysis (complete case analysis), or replace the missing/outlier values by mean estimates based on the data (mean imputation).

Developing and updating AI models and implementation requires considerable financial resources (for software, hardware, and training), which poses challenges for their integration into health care systems. Potential cost-saving solutions include strategic adoption, cloud-based services (delivered over the Internet), and partnering with experienced AI vendors (Supplemental Figure 2). Clinical adoption may be hindered by the limited interpretability of complex AI models, which have been likened to "black boxes," and the limited transparency into AI decision-making that may undermine trust. Lowincome countries face challenges in harnessing the benefits of AI, exacerbating global disparity in technology adoption. To achieve AI catch-up, low-income countries need to address challenges related to digital infrastructure, human capital, and commercialization. Organizations such as OpenAI aim to help low-income countries develop AI infrastructure. Developing countries could particularly benefit from AI-empowered auscultation, ECG, and echocardiography to improve the diagnosis of VHD despite unavailability of more advanced cardiac imaging technologies.

Ethical concerns such as data privacy and patient consent should also be considered. Increased regulations around AI hinder adaptation and data exchange for model training and testing. One option to circumvent this issue and enhance data security is federated learning, whereby the data remain in the hospital, but the algorithm is trained in a distributed way concurrently in different sites.⁷⁴ This concept has already been successfully demonstrated in a network of 8 hospitals providing more than 8,000 CTs for automated aortic valve analysis and calcification assessment before TAVR.⁷⁵ However, federated learning faces issues related to its complex implementation and cannot fully resolve privacy concerns.⁷⁶

Another critical issue is uncertainty around liability in case of erroneous AI decision-making, especially if it affects a patient. It remains unclear whether accountability lies with the developer, physician, company, or hospital. Another limitation includes possible overreliance on AI translating into loss of expertise and inadequate handling of complex cases. Automatic generation of management

decisions may seem less desirable than a human network engaging with the clinical, personal, environmental, and social aspects of each patient. Therefore, although AI can be a powerful tool to improve outcomes and reduce workflow, it should not replace human clinical insight and oversight.

CONCLUSIONS

By using the full potential of AI, clinicians can provide a robust, personalized management strategy for patients with VHD, with enhanced risk prediction, decision-making, procedural success, and outcomes. At present, challenges for fully integrating AI into clinical practice include potential biases, concerns about reproducibility and data privacy, and the considerable resources required. Addressing these concerns will ensure that AI-based technologies are used safely and responsibly in the transition to digital health care.

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APPENDIX For supplemental figures and table and a video of the interactive Central Illustration, please see the online version of this paper.