Perspective

New concepts for mitral valve imaging

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The high complexity of the mitral valve (MV) anatomy and function is not yet fully understood. Studying especially the dynamic movement and interaction of MV components to describe MV physiology during the cardiac cycle remains a challenge. Imaging is the key to assessing details of MV disease and to studying the lesion and dysfunction of MV according to Carpentier. With the advances of computational geometrical and biomechanical MV models, improved quantification and characterization of the MV has been realized.

Geometrical models can be divided into rigid and dynamic models. Both models are based on reconstruction techniques of echocardiographic or computed tomographic data sets. They allow detailed analysis of MV morphology and dynamics throughout the cardiac cycle. Biomechanical models aim to simulate the biomechanics of MV to allow for examination and analysis of the MV structure with blood flow. Two categories of biomechanical MV models can be distinguished: structural models and fluid-structure interaction (FSI) models.

The complex structure and dynamics of MV apparatus throughout the cardiac cycle can be analyzed with different types of computational models. These represent substantial progress in the diagnosis of structural heart disease since MV morphology and dynamics can be studied in unprecedented detail. It is conceivable that MV modeling will contribute significantly to the understanding of the MV.

Keywords: Mitral valve (MV); geometrical model; structural model; fluid-structure interaction model; mitral valve imaging

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Introduction

Profound anatomical and pathophysiological knowledge of the mitral valve (MV) and adjacent cardiac structures are essential for selecting the most appropriate surgical techniques in MV disease, especially with regards to modern minimally-invasive MV surgery and transcatheter approaches (1-4). Imaging is the key to assessing details of MV disease and to studying the lesions and dysfunction of MV according to Carpentier (5).

Imaging enables assessment of MV function, especially morphological and dynamic basics throughout the cardiac cycle, with particular consideration of the respective pathology (6). Thus, imaging is essential for decision-making and treatment planning.

While multiple modalities exist to assess MV, transthoracic echocardiography (TTE) represents the standard technique to study MV disease (6). Especially with current advances of 3-dimensional (3D) echocardiography in combination with multi-detector row computed tomography (MDCT) and cardiac magnetic resonance (CMR), improved characterization and quantification of the MV apparatus and its functional complexity has improved significantly (7-9). Most recently, geometrical and biomechanical models for analysis of MV are undergoing very early clinical evaluation (10-13).

This perspective article reports on several new concepts of MV modeling specified for MV evaluation and treatment planning.

Table 1 Anatomic structures of mitral valve complex (15)

Mitral valve complex
Mitral valve
Valvular leaflets and commissures
Annulus
Subvalvular apparatus with
Tendinous cords
Papillary muscles
Left atrial myocardium
Left ventricular myocardium
Left atrial and left ventricle endocardium
Aorto-mitral curtain

MV anatomy and physiology

Imaging of the MV apparatus requires a detailed understanding of the anatomy and physiology (14). This is of utmost importance for clinical evaluation and subsequent surgical and/or interventional treatment. Numerous clinical and anatomical data have been collected thus far describing the MV as a complex of several adjacent structures which collectively constitute the MV complex (*Table 1*) (15,16). The normal function of the MV depends on the coordinated action of several interrelated anatomical elements: the left atrium (LA), the anterior and posterior leaflets, the annulus, the chordae tendineae, the papillary muscles and the left ventricular wall (15). It is of note that each of those components is important, as any alteration or lesion may cause MV dysfunction (stenosis, regurgitation) (6). Structural MV abnormalities are referred to as organic or structural MV disease. Dysfunction of the MV, which evolves secondarily to left ventricular dilatation, is referred to as functional MV disease (6). For the assessment of MV, morphological and functional indices have been established.

With regards to the complexity of MV, it is generally accepted that the physiology and pathophysiology of the MV apparatus, defined as a nonlinear system of fluid-structure interaction (FSI), are at present not fully understood (17).

Computational MV models

Computational models are defined as mathematical models in computational science that require computer simulation and thus computational resources to study the functionality of any complex system. Study objects are complex nonlinear systems for which simple and intuitive analytic solutions are not readily available. Rather than deriving a mathematical analytical solution from a given problem, experimentation with computational models is done by adjusting the parameters of the system in a stepwise fashion in order to achieve a definite approximation.

A scientific model seeks to represent a physical process in a logical and objective manner. Therefore, the process of generating a model is primarily based on key factors influencing a defined physical process. In models, real physical processes are abstracted, reduced or aggregated. Models are typically used when it is either impossible or impractical to create experimental conditions in which scientists can directly measure outcomes.

The creation of computer models in cardiovascular medicine requires close collaboration between physicians, computer scientists and engineers. In cardiovascular medicine, one can distinguish between different types of computational models such as geometric models, biomechanical models and multi-scale generic models. All models are based on the actual anatomic structure and are developed to fulfil very special requirements (*Figure 1*). It is important to acknowledge that increasing complexity increases the calculation time of the model. The most commonly used models in cardiovascular medicine are geometrical models and biomechanical models. Past studies have shown that these models are suitable for the description of complex morphological and biomechanical changes of the heart and great vessels. Computational models were used for accurate analysis of left and right ventricular contraction, flow simulation through artificial heart valves or shear stress analysis of the aorta with aortic aneurysms (17-22).

Exact modeling of MV function has not been realized in the past due to the lack of imaging techniques that enable detection of the 3D structures and their respective function. With the development of real-time 3D echocardiography (RT3DE) and 4-dimensional computed tomography (4DCT), however, the technical capabilities have been introduced to create substantial and well-defined MV models with a high probability for implementation into clinical practice (11).

Geometrical MV models

Substantial progress in surgical and percutaneous treatment of structural MV disease has reinforced the interest in non-invasive quantitative analysis of MV morphology and function. Precise morphological and functional knowledge about the MV is a prerequisite during the entire clinical

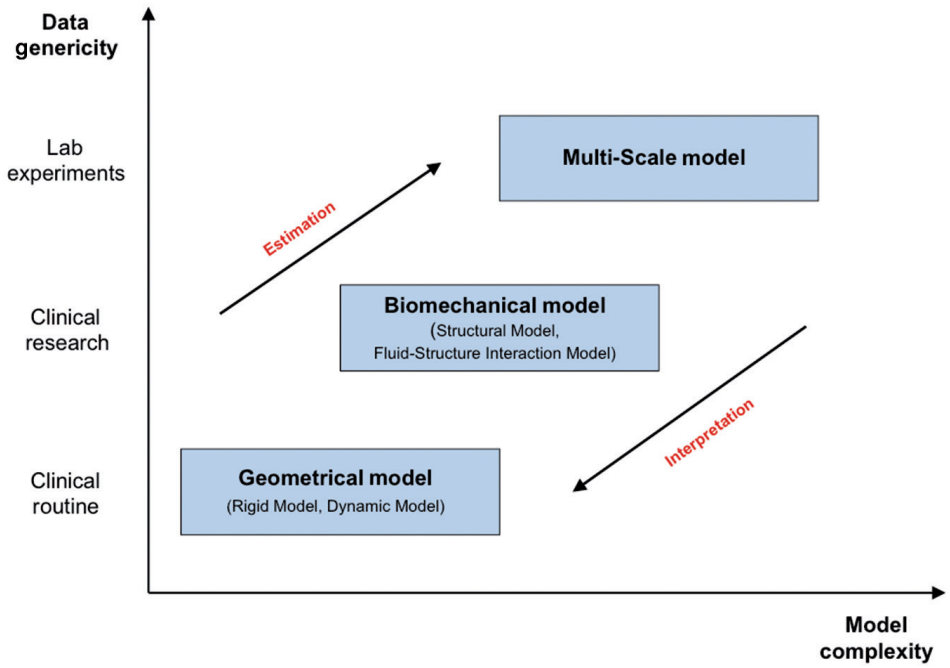

Figure 1 Overview of different types of MV models depending on complexity and type of data. Geometrical and biomechanical models are currently the most suitable for integration in clinical routine and research.

workflow, including diagnosis and therapy planning (11). Currently, most non-invasive MV imaging techniques are based on 2D methodology, such as echocardiography or CT (*Figure 2*). Due to the complexity and dynamics of MV, accurate geometrical analysis of MV from 2D data sets using echocardiography or CT is difficult. With the introduction and increasing use of RT3DE and 4DCT, it is possible to detect comprehensive structural and dynamic information, including quantification of the MV throughout the cardiac cycle (23,24). Furthermore, with the introduction of imaging-based computational MV models, improved quantification and characterization of the MV has been realized (12,13).

The main objectives of MV modeling are (11):

(I) Robust conversion of imaging data sets into a virtual model which results in physiological modeling;

(II) Patient-specific assessment;

(III) Model-based quantification and visualization.

In addition, this provides an opportunity for interactive manipulation, including rotation, translation, adjustment, zoom, rendering, 2D and 3D measurements.

Rigid MV models

Rigid models are basically only static reconstructions of the MV, the principles of which have been described before (12,13). This technology is generally described as segmentation: after importing a 3D data-set, detection of major anatomic landmarks is conducted with subsequent surface modeling using a geometric mesh. Morphological quantification of MV can be computed according to the final model.

The two most commonly used software systems for MV analysis are the Mitral Valve Quantification (MVQ) program (Philips Healtcare, Inc., Andover, MA, USA) and the 4D MV assessment software (TomTec Imaging Systems GmbH, Munich, Germany) (12,13,23,25). The clinical impact of MV models is still being evaluated but their contribution to the description of MV physiology and pathophysiology is thus far undisputed (23). Rigid models have mainly been used to study dimensions of the mitral annulus in ischemic, non-ischemic and myxomatous MV disease (17,26,27). Of particular interest has been the mitral annulus after MV repair and the influence of aortic valve replacement on the mitral annulus geometry (27,28). Unfortunately, existing rigid models are limited due to static measurements at a predefined phase of the cardiac cycle, which are being performed by manual segmentation, thus preventing further development (12,13,25).

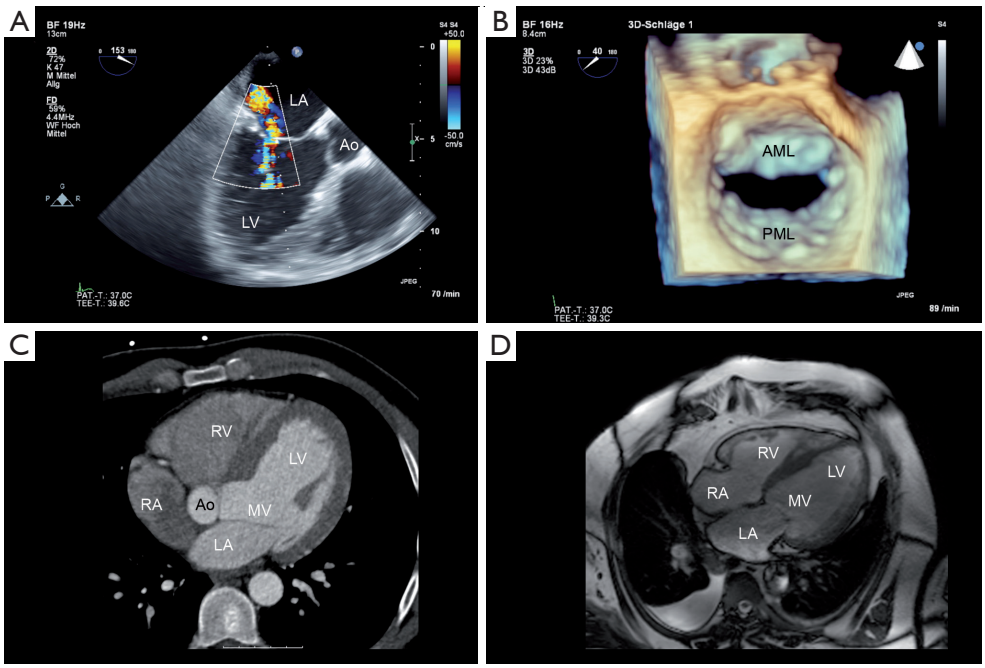

Figure 2 Different modalities for MV imaging. (A) 2D echocardiography with colour Doppler flow; (B) 3D transesophageal echocardiography; (C) Computed tomography; (D) Magnet resonance imaging. AML, anterior mitral leaflet; Ao, Aorta; LA, left atrium; LV, left ventricle; MV, mitral valve; PML, posterior mitral leaflet; RA, right atrium; RV, right ventricle.

Dynamic MV models

It is widely accepted that the MV is a highly complex dynamic structure, which is directly related to hemodynamic changes subsequent to muscle contraction of the left ventricle throughout the cardiac cycle (29). Using dynamic MV models, the morphology and dynamics of MV can be reconstructed from 4D data sets, such as full volume RT3DE data, over the entire cardiac cycle. Considering the complexity of MV, the necessary estimation procedure of dynamic MV models can be divided into two tasks (11):

(I) Object delineation;

(II) Motion estimation.

In the dynamic MV model presented herein (AutoValve Beta 10.0, Siemens Corporate Research, Princeton, USA), the modeling is hierarchically defined on three abstraction levels (11):

(I) Estimation of a global location of MV within a given imaging data set and segmentation of a rigid landmark motion model;

(II) Estimation of a non-rigid landmark motion model;

(III) Estimation of a mitral comprehensive model.

This method of MV dynamic modeling applying this algorithm has been described before (*Figure 3*) (10,11). With this model, different quantitative MV parameters, including annular circumference, leaflet area and mitral orifice area, are continuously depicted over the entire cardiac cycle (*Table 2*). It is important to note that the quantification potential of the proposed method is not limited. Through the consistent and comprehensive spatial and temporal representation, the introduced system offers unique analytic features, which facilitate decisions during the whole clinical workflow.

Currently, echocardiographic-based dynamic MV models are in the phase of early clinical validation. It can be expected that in the near future, dynamic MV models will significantly improve the assessment of the MV and therefore may substantially contribute to the understanding of the MV complex.

Model-based quantification of MV

Different specific data on morphological and functional parameters of the MV complex can be derived from MV models (*Figure 4*). Although not clinically implemented,

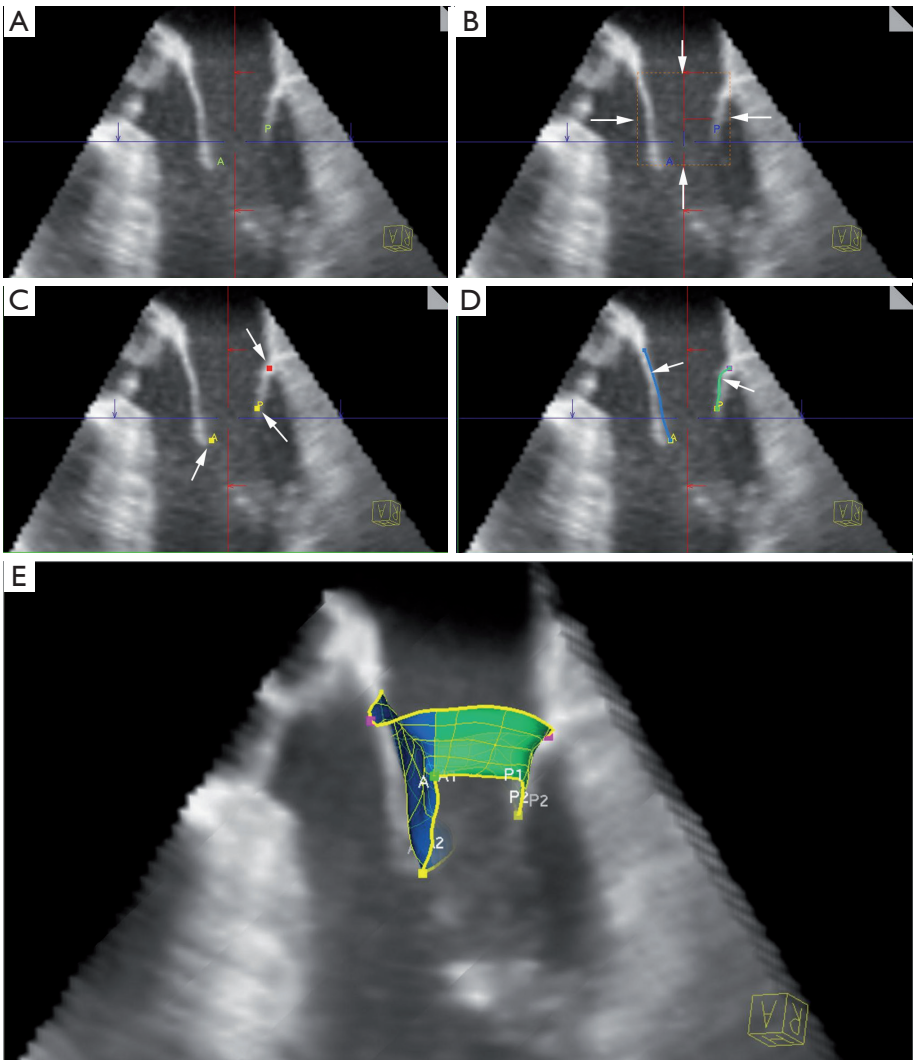

Figure 3 4D MV model estimation algorithm. (A) RT3DTEE data set; (B) Global location of MV; (C) Landmark detection (yellow—posterior and anterior leaflet tips; red—annulus); (D) Surface model (blue—anterior leaflet; green—posterior leaflet); (C) Comprehensive MV model.

several benefits of such a model are (11):

(I) Increased level of precision, especially when studying native three-dimensional valve anatomy;

(II) High reproducibility due to automatic quantification;

(III) User independence;

(IV) Functional assessment throughout the cardiac cycle;

(V) Comprehensive analysis, including complex morphology such as curvatures, deformation fields and volumetric variations.

Comprehensive valve measurements are important in regards to clinical workflow among cardiac surgeons, especially for treatment planning in percutaneous and minimally-invasive valve interventions, which require extensive non-invasive assessment. Thus MV modeling is likely to contribute most significantly to assessing the type of MV repair, the level of MV disease complexity, and improving decision-making.

Biomechanical MV models

Biomechanical and fluid dynamic analysis of the MV complex is a prerequisite in understanding MV function. While geometrical models focus on morphological and dynamic quantification of MV, biomechanical models aim to simulate the biomechanics of MV (structural models) to allow for examination and analysis of the MV structure with

Table 2 Variables computed from the geometrical mitral valve model throughout the cardiac cycle

Parameters
Mitral annulus
Anteroposterior diameter
Anterolateral-posteromedial diameter
Intercommissural diameter
Annular area
Annular circumference
Annular height
Annular height to commissural width ration (AHCWR)
Sphericity index
Annular non-planarity angle
Annular deviation ratio
Leaflets
Mitral valve orifice area (2D/3D)
Coaptation depth
Coaptation length
Commissural width
Tenting area and volume
Posterior and anterior leaflet length
Posterior and anterior leaflet angle

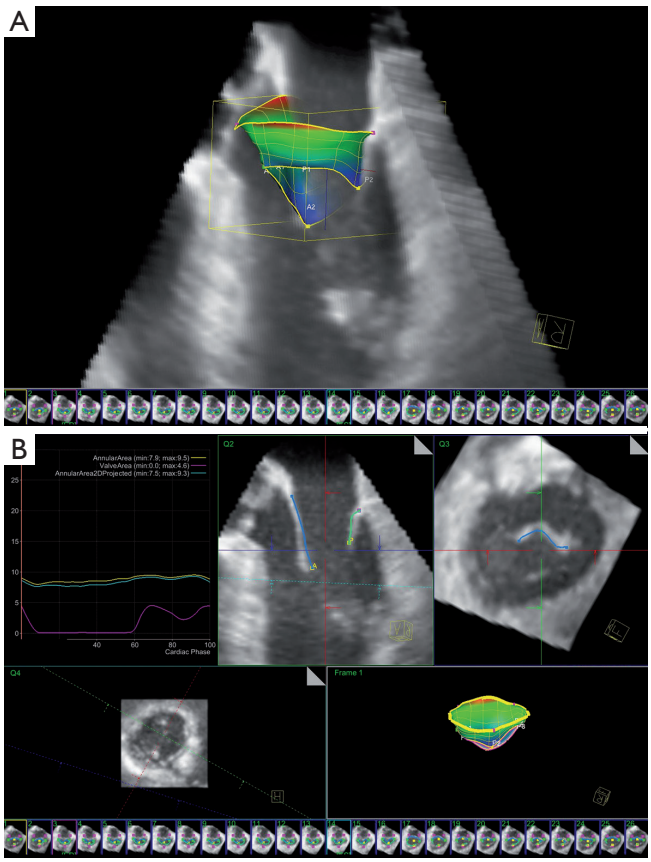

Figure 4 4D MV model. (A) Physiological model of MV within RT3DTEE data set; (B) Example for model-driven annulus and valve measurements throughout the cardiac cycle and different options for MV visualization.

blood flow (FSI models). It is therefore a basic necessity to accurately assess MV and left ventricle geometry as depicted in the respective geometric models. Furthermore, biomechanical models are particularly challenging with regards to numerical algorithms that represent MV complexity as well as computational resources. Pioneering work has been presented by Kunzelmann *et al.* in which newly proposed models allow for detailed insights on MV function (30-32). Two categories of biomechanical MV models can be distinguished: structural models and FSI models. Previous studies have shown that structural models are more reliable for simulation of static events, but in order to accurately simulate full dynamic behaviour, FSI models are required (33).

Structural MV models

Structural models aim to simulate the biomechanics of MV without directly taking into account the blood flow (34). The most widely used model type for cardiac structures is the finite element method (FEM), a numerical approximation technique for boundary value problems. The mathematical algorithm involves accurate geometry, surface pressure and boundary conditions such as material properties and other aspects of the MV apparatus. Using FEM, shear stress of the leaflets or annulus, deformation of MV geometry throughout the cardiac cycle, or disease progression can be simulated (*Figure 5*) (31,35). Furthermore, it is possible to simulate—at a preliminary stage—surgical or interventional MV procedures (32,34).

MV leaflets, annulus and chordae have been identified as non-linear tissue with anisotropic linear elasticity (30,34,36). MV biomechanics is mostly modelled using hyper-elasticity theory (37). These methods enable simulation of leaflet and annulus stress distribution during MV motion, as well as annular contraction (37-42). One example of simulation is MV edge-to-edge repair, a prominent repair technique in contemporary MV treatment (34).

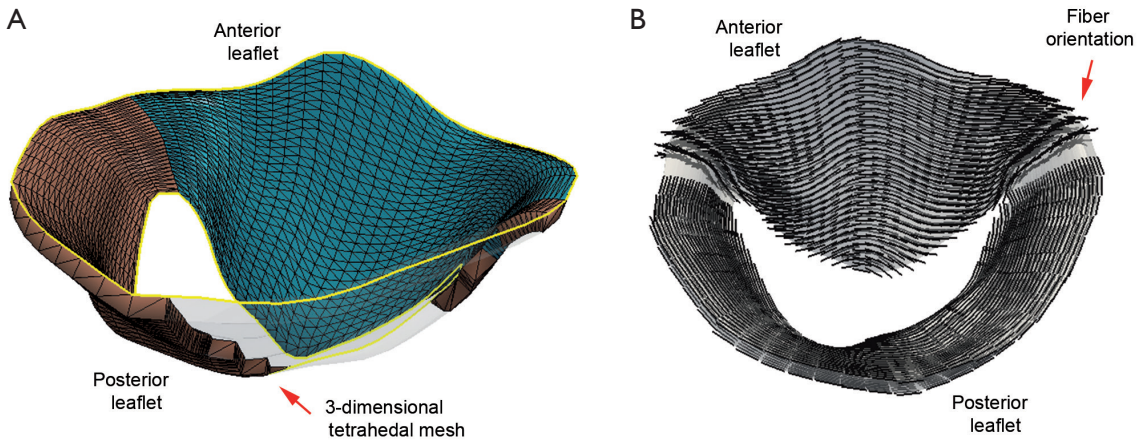

Figure 5 Structural models of MV. (A) 3-dimensional tetrahedal mesh of MV leaflets; (B) Structural model of MV fiber orientation. Fibers are oriented parallel to the annulus. Fibers become radial close to commissures.

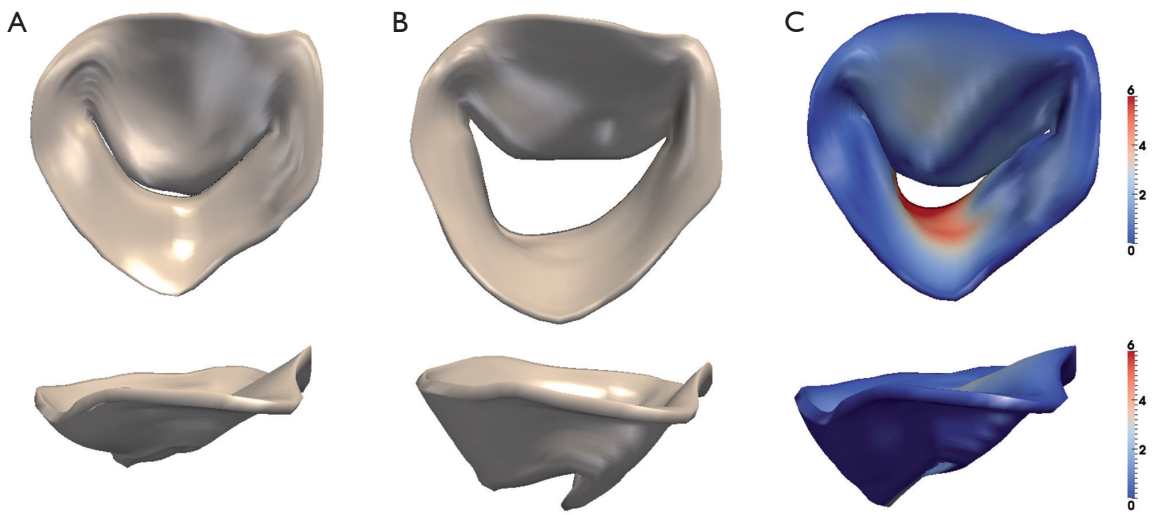

Figure 6 Simulated MV closure in one patient with a structural MV model. (A) Closed MV; (B) Open MV; (C) MV during diastole with point-to-mesh distance to ground truth (in mm).

Structural models are currently under clinical investigation in selected research projects (*Figure 6*). With the improvement of technology, integration into a clinical routine can be expected.

Structure-fluid interaction models

Fluid-structure models aim to study the interaction between the MV and the blood flow. In such models, a structural model of the MA (FEM) is combined with a computational fluid dynamic (CFD) model. This allows for analysis of flow and dynamic structures. These models currently represent the most complex modelling type.

Such models analyze the direction of blood flow, blood flow rate, blood flow volume and blood pressure while simultaneously simulating the influence of blood flow on the surrounding structures of the MV. In the last decade, initial algorithms have been established for structure-fluid interaction modelling. Using such technology, a MV specimen can be investigated in a standardized liquid environment such as a tube, box or an idealized left ventricle (33,43). However, any standardized model poorly reflects human anatomy of the LA and left ventricle (44). Nevertheless, FSI models represent thus far the most comprehensive analysis of the MV.

Limitations of computational models

Geometrical models

Geometrical models are mostly based on RT3DE data sets. Accordingly, the limitations of RT3DE also apply for geometrical models. These are R-wave gating and the existence of modeling based on a non-continuous cardiac cycle. Patient-specific modeling is highly time consuming due to visual inspections and manual corrections of landmarks.

Biomechanical models

Structural and FSI models have limitations such as calculating only one level of thickness of the MV leaflets, since they are based on linear calculation algorithms. It also requires costly computational power and time. FSI models are based on non-physiological rigid and static boundaries.

Conclusions

The complex structure and dynamic of MV apparatus throughout the cardiac cycle can be analyzed with different types of computational models. These represent substantial progress in the diagnosis of structural heart disease since MV morphology and dynamics can be studied in unprecedented detail. It is undoubtedly conceivable that MV modeling will contribute to a deeper understanding of the MV.

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