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FROM CARDIOMYOPATHY TO HEART FAILURE: INSIGHTS FROM COMPUTATIONAL MODELS OF LEFT HEART VENTRICLE

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Abstract

This study presents the use of computational modeling to improve understanding of hypertrophic cardiomyopathy (HCM) and its progression to heart failure. A review of related work highlights advances and challenges in computational modeling and integration of clinical data for model development and validation. Using parametric model of the left heart ventricle, the multiscale Fluid-Solid Interaction (FSI) is performed within the PAK Finite Element (FE) software, simulating cardiac cycles in two patients with clinically diagnosed HCM, and analyzing biomechanical parameters such as pressure, velocity, displacement, and pressure-volume (PV) loops. The results show strong agreement with clinical data, particularly for left ventricular ejection fraction (LVEF). Our findings demonstrate the value of computational tools for patient-specific, non-invasive assessment of cardiac function and disease progression. Continuous development of PAK software and its integration with clinical data will further enhance its role in cardiovascular research, supporting diagnosis, treatment planning, and personalized care in cardiomyopathies and heart failure.

Keywords: heart failure, cardiomyopathy, computational modeling, finite element analysis, PAK software

1. Introduction

Heart failure is a serious and growing health problem worldwide. It occurs when the heart cannot pump enough blood to meet the body's needs which can lead to fatigue, shortness of breath, swelling in the legs, and other symptoms that reduce a person's quality of life. In more serious cases, heart failure can become life-threatening (Ponikowski et al., 2016). The number of people living with heart failure is rising, partly due to aging populations and better survival after heart attacks or other heart diseases. It affects an estimated 64 million people globally and contributes significantly to hospitalizations and high health care costs (Groenewegen et al.,

2020; James et al., 2018; Roth et al., 2018; Savarese & Lund, 2017). Approximately 6.7 million people in the United States over 20 years of age have heart failure, and the prevalence is expected to rise to 8.5 million Americans by 2030 (Bozkurt et al., 2023). The annual cost of caring for a heart failure patient in the United States is approximately $30,000, with estimates varying widely in other countries (Heidenreich et al., 2022). Heart failure also carries a high risk of death. In many cases, the five-year survival rate is lower than for some cancers (Benjamin et al., 2019). Due to these challenges, finding better ways to understand, detect, and treat heart failure is a major priority in medicine today.

One of the main causes of heart failure is cardiomyopathy, a group of diseases that directly affect the heart muscle. Cardiomyopathies change the structure and function of the heart, making it weaker or stiffer over time. As the disease progresses, the heart can no longer work properly, which may eventually lead to heart failure (Bozkurt et al., 2016). Direct causes of cardiomyopathy include pathological gene variants (mutations), toxins, autoimmune diseases, infections, and tachycardias. Disease modifiers, conditions that can exacerbate or trigger cardiomyopathy, include epigenetic factors and acquired modifiers, such as pregnancy and most cardiovascular diseases. This crucial interaction between genetic and acquired disease causes is important to consider when diagnosing cardiomyopathy (Bondue et al., 2018). The identification of acquired causes of cardiomyopathy does not exclude latent pathogenic genetic variants, although these may require additional acquired causes and/or disease modifiers to manifest clinically. The most common causes and modifiers of cardiomyopathy are: genetic mutations, neuromuscular disorders, syndromic disorders, acquired diseases, comorbidities with possible interaction with genetic mutations (Baumgartner et al., 2021).

There are different types of cardiomyopathies, including:

- **Dilated cardiomyopathy (DCM)** – where the heart becomes enlarged and its pumping ability is reduced;
- **Hypertrophic cardiomyopathy (HCM)** – where the heart muscle becomes abnormally thick, making it harder for the heart to fill with blood;
- **Restrictive cardiomyopathy (RCM)** – where the heart muscle becomes stiff and cannot relax properly;
- **Arrhythmogenic right ventricular cardiomyopathy (ARVC)** – which affects the heart's electrical system and can cause irregular rhythms and sudden cardiac death (Maron et al., 2006).

Each of these types can lead to heart failure in different ways, depending on the underlying changes in heart structure, function, and electrical activity. Understanding how cardiomyopathies develop and progress toward heart failure is crucial for several reasons.

First, early and accurate clinical diagnosis is essential. Cardiomyopathies often remain undetected until the disease has significantly advanced or complications occur. In many cases, subtle symptoms or changes on an electrocardiogram or imaging can be the first signs. Recognizing these signs early allows for timely interventions that may slow or even prevent progression to heart failure (Elliott et al., 2008; Hershberger et al., 2018).

Second, selecting the right treatment depends on correctly identifying the type and cause of cardiomyopathy. For instance, HCM may benefit from medications that reduce heart contractility, while DCM may require drugs that improve pump function or prevent dangerous arrhythmias (Bozkurt et al., 2016; Ommen et al., 2020).

Finally, predicting patient outcomes helps guide long-term management and monitoring strategies, which nowadays includes novel technologies, such as artificial intelligence (AI),

voice as a biomarker ant other clinical data (Nahar & Lopez-Jimenez, 2022). Knowing which patients are at higher risk for sudden cardiac death, arrhythmias, or rapid heart failure progression enables clinicians to offer more personalized care. In patients with advanced heart failure, decisions regarding the implementation of implantable devices such as defibrillators and the consideration for advanced therapies like heart transplantation are critical components of management strategies (Algalarrondo et al., 2018; Maron et al., 2014).

Altogether, improved understanding of the relationship between cardiomyopathies and heart failure supports a more personalized, predictive, and preventive approach to cardiac care. It is in this context that computational models can play an important role, offering deeper insight into disease mechanisms and helping to bridge the gap between biological understanding and clinical decision-making (Corral-Acero et al., 2020).

In recent years, computational modeling has become a valuable tool in cardiovascular research. These models simulate the behavior of the heart under normal and pathological conditions. They allow researchers to explore how changes in the heart's structure, mechanics, or electrical properties can lead to disease progression (Saveljic & Filipovic, 2022). This is especially important in cardiomyopathies, where the underlying mechanisms are complex and often not fully understood. By using computational models, researchers can test hypotheses, perform virtual experiments, and investigate scenarios that would be difficult or impossible to study in real patients (Pathmanathan & Gray, 2013; Trayanova & Winslow, 2011).

Computational models vary in their level of detail. Some focus on the cellular or molecular level, modeling processes such as calcium handling or ion channel dynamics (Clayton et al., 2011). Others simulate the whole organ, capturing the electrical activation, mechanical contraction, and blood flow within the heart (Niederer et al., 2019). Some models are even patient-specific, built from medical images or clinical data to represent an individual's unique heart structure, function and response to selected medical treatment (Tomasevic et al., 2023). This approach is known as personalized or precision modeling, and it has the potential to support diagnosis, risk prediction, and treatment planning in the future (Corral-Acero et al., 2020).

In the context of cardiomyopathies, computational modeling can help identify how specific genetic mutations or structural abnormalities lead to changes in heart performance (Zhang et al., 2023). It can also simulate how the heart compensates over time and which factors eventually lead to decompensation and heart failure. For example, models have been used to study how increased wall stress in DCM affects muscle strain, or how thickened walls HCM change the electrical conduction pathways and lead to arrhythmias (Augustin et al., 2016; Margara et al., 2021). Moreover, the growing use of multiscale and multiphysics modeling allows integration of different systems – from genes to organs, providing a more complete picture of heart disease. These tools are not only advancing research but are also moving toward clinical application, thanks to improvements in computational power and software accessibility (Quarteroni et al., 2017; Trayanova et al., 2024; Trayanova & Boyle, 2013; Trayanova & Rice, 2011).

In this review, the use of computational models to study cardiomyopathies, specifically HCM, is explored, along with how these morphological and functional changes can lead to heart failure. An overview of important modeling techniques, key results, and the current challenges in the field is presented. Especially, the capabilities of PAK software (*PAK Finite Element Software*, 2025) in multiscale simulation of heart behavior are presented, aiming to show how computational tools can support better understanding and management of heart failure caused by cardiomyopathy.

The paper is structured as follows. Section 2 covers related work in the field, including computational modelling in cardiomyopathies and heart failure, Finite Element Analysis (FEA)

and AI in cardiovascular modeling, the use of medical data for model development and validation, existing platforms and models in cardiomyopathy and heart failure research, and, finally, current challenges. Section 3 describes the materials and methods used to model the parametric left ventricle with HCM and to computationally simulate two health states for two selected patients, using the PAK FE software. Section 4 presents and discusses the main results, including pressures, velocities, and displacements of the HCM models during the cardiac cycle, as well as Pressure-Volume (PV) diagrams and comparisons with clinical findings. Section 5 summarizes the main conclusions of the study and outlines future improvements and challenges.

2. Related work

Computational modeling has become an invaluable tool for understanding the complex mechanisms behind cardiovascular diseases, particularly cardiomyopathies and heart failure. In recent years, advances in multiscale modeling, FEA and AI have enabled the development of more accurate, predictive, and patient-specific models. These models are becoming critical in guiding clinical decision-making, testing new treatments, and evaluating disease progression. In this section, the computational models of different types of cardiomyopathies, their role in heart failure, the integration of medical data for model development and validation, the existing platforms and models, together with current challenges will be summarized.

2.1 Computational Modeling in Cardiomyopathies and Heart Failure

The application of computational models in understanding cardiomyopathies has been a significant area of research. Cardiomyopathies, which include DCM, HCM, RCM, and ARVC, each exhibit distinct pathophysiological mechanisms. As such, models need to account for the specific changes in myocardial structure and function associated with each type of cardiomyopathy (Maron et al., 2012). Several studies have focused on the development of multiscale computational models that combine biological, mechanical, and electrical systems to study heart function in diseases like HCM and DCM (Pathmanathan & Gray, 2013; Trayanova & Rice, 2011). For example, the electromechanical models have been used to study the HCM and its drug response at the cardiomyocyte level (Liu et al., 2023). Also, in the analysis of HCM altered myocardial tissue structure and abnormal mechanical properties lead to the thickening of the heart walls and impaired blood flow (D. Nordsletten et al., 2011; D. A. Nordsletten et al., 2011). These models incorporate both the electrophysiological activity and the mechanical response of the myocardium, which is critical for understanding arrhythmias and heart failure progression. In the case of DCM, models have explored the effects of increased chamber size and reduced myocardial contractility applying strong electromechanical coupling, which can lead to altered pumping efficiency and subsequent heart failure (Lee et al., 2023).

By simulating structural and functional changes, researchers have been able to identify potential therapeutic targets, such as drugs that modify contractile function, by applying computational modeling in both HCM and DCM cardiomyopathies (Mijailovich et al., 2022). In the area of drug discovery and drug design approaches, computational modeling can speed up this process and significantly reduce expenses aiming to improve the treatment of cardiomyopathy, which is presented in recent study related to computational modeling on drugs effects for left heart ventricle in HCM and DCM, using both experimental and patient-specific clinical data for development and validation of suggested method (Tomasevic et al., 2023).

2.2 Finite Element Analysis and AI in Cardiovascular Modeling

Finite Element Analysis (FEA) has also been widely employed to model the mechanical properties of heart tissue and the interactions between different layers of the myocardium, blood vessels, and valves. FEA allows for high-resolution, three-dimensional (3D) simulations of myocardial deformation, which is crucial for studying cardiomyopathies that involve significant structural changes (Mojumder et al., 2023). These simulations can model tissue behavior under various conditions, such as increased wall stress or altered loading conditions, helping to predict how these structural abnormalities contribute to heart failure (Niederer et al., 2019).

Of particular interest is the computer simulation of Fluid-Solid Interaction (FSI), which mainly uses weak or strong coupling (Landajuela et al., 2017) as well as the mixed Lagrangian-Eulerian (ALE) formulation (Donea et al., 2017). Electrical signals affect the change in calcium concentration within the muscle cells of the heart tissue, which leads to contractions of the walls. In simplified models, the calcium concentration is given as an input function. Such models find application in cardiac pathologies associated with diastolic filling (de Vecchi et al., 2013). Complex computer models of the heart include a coupled fluid-solid-electro-mechanical model (Santiago et al., 2018). If electrical depolarization is not taken into account, FSI models are used to describe the diastolic phase (Cheng et al., 2005; Domenichini et al., 2005; H. Gao et al., 2014; Kovács et al., 2001), while the input function of calcium concentration is used to generate the active voltage during systole (Chen et al., 2016; D. Nordsletten et al., 2011).

In addition, the integration of artificial intelligence (AI) and machine learning (ML) techniques into computational models of heart failure has become increasingly important. The AI and ML can assist in analyzing large, complex datasets from patients with cardiomyopathies, helping to identify patterns that are not immediately visible through traditional methods (Pičulin et al., 2022; Smole et al., 2021). In particular, AI-driven models can enhance personalized modeling by integrating patient-specific data, such as genetic information, clinical images, and electrophysiological data, to generate more accurate predictions of disease progression and treatment outcomes (Corral-Acero et al., 2020; Mohsen et al., 2023).

2.3 Medical Data for Model Development and Validation

The development of accurate computational models depends heavily on the integration of diverse medical data sources. In particular, imaging data (e.g., MRI and CT scans), electrophysiological measurements (e.g., ECG, intracardiac mapping), and genetic data are invaluable for building personalized models. Recent advances in medical imaging have enabled the creation of patient-specific models, where the heart's geometry and tissue properties are derived directly from scans, providing high-resolution simulations that closely resemble the actual heart (Davey et al., 2024). This integration of patient-specific data is essential for model validation, as it ensures that the simulations accurately reflect the real-world conditions of the patient’s heart (Galappaththige et al., 2022).

Furthermore, genetic data plays a crucial role in linking cardiomyopathies to specific mutations. By incorporating genetic data into computational models, researchers can better understand how mutations in genes like MYH7 (which encodes for cardiac myosin) or TNNT2 (which encodes for cardiac troponin T) contribute to disease development (Hershberger et al., 2013, 2018; Marian & Braunwald, 2017). These models, therefore, provide valuable insights into genotype-phenotype correlations, helping to identify which patients may benefit from specific treatments or interventions (Mijailovich, Prodanovic, Poggesi, Powers, et al., 2021).

2.4 Existing Platforms and Models Supporting Cardiomyopathy and Heart Failure Research

Several computational platforms have been developed to support the modeling and simulation of heart disease. Among the first is the Cardiac Atlas Project providing a comprehensive database of 3D heart models that can be used for research and clinical applications (Fonseca et al., 2011). These models have been used to simulate various heart conditions, including heart failure, and to explore how different treatments might impact heart function. Furthermore, platforms like OpenCARP (Plank et al., 2021) and Chaste (Cooper et al., 2020) provide open-source tools for creating and simulating cardiovascular models, enabling researchers worldwide to build on existing models and contribute to the development of more accurate simulations.

In recent years, many computational platforms for *in silico* testing have been developed. One of them is SILICOFCM platform [(*SILICOFCM H2020 Project: In Silico Trials for Drug Tracing the Effects of Sarcomeric Protein Mutations Leading to Familial Cardiomyopathy*, 2022)] for *in silico* clinical trials, testing the effectiveness of pharmacological treatment for left heart ventricle performance, in case of different types of cardiomyopathies (Filipovic, Saveljic, et al., 2022; Filipovic, Sustersic, et al., 2022). This platform is result of EU Horizon 2020 founded project, spanning partners across Europe and USA. It integrates patient-specific data and allows the testing and optimization of medical treatment for maximized positive therapeutic outcomes. The integrated biological, genetic, clinical and imaging data are processed using different tools in the area of bioinformatics, machine learning, data analytics, multiscale modelling, and FE modelling.

One of platforms which is currently being developed is the INTELHEART platform designed to address the challenges of diagnosing and managing heart failure through a personalized approach (*Artificial INTELligence-Based Decision Support System for Early and Accurate Diagnosis of HEART Failure - the INTELHEART Project*, 2025). It utilizes a wide range of patient-specific data (electronic health records, imaging data, lab tests, clinical history, voice as a biomarker, psychological tests) and applies ML algorithms to improve diagnostic accuracy and detect early indicators of heart failure. In addition to aiding diagnosis, INTELHEART helps clinicians create individualized treatment strategies that can evolve with the patient's condition, aiming to minimize rehospitalizations and support proactive care. Positioned at the crossroads of cardiology and AI, the AI-powered Decision Support System (DSS) such as INTELHEART demonstrates how AI-based solutions can not only enhance clinical outcomes but also mitigate the significant financial burden heart failure places on healthcare systems (Tomasevic et al., 2024).

2.5 Current Challenges

Despite these advancements, several challenges remain in the field of computational modeling for cardiomyopathies and heart failure. One of the primary obstacles is the heterogeneity of the disease, both at the patient level and in terms of disease progression. As heart failure can result from various etiologies and mechanisms, it is difficult to develop universal models that can accurately predict outcomes for all patients (Bozkurt et al., 2016; Maron et al., 2014).

Another challenge is the integration of multimodal data. While medical data such as imaging and genetic information are critical for model accuracy, integrating these different data types into a unified framework remains complex. Differences in data resolution, variability across patients, and the sheer volume of data can complicate the creation of robust models (Hershberger et al., 2013, 2018).

Finally, while patient-specific models hold great promise, the computational cost of creating and simulating these models can be prohibitively high. Large-scale simulations require

substantial computing power and time, which limits their clinical scalability and widespread adoption (Niederer et al., 2019; Trayanova & Rice, 2011; Trayanova & Winslow, 2011).

In addition to computational demands, there are significant challenges related to model validation and regulatory approval. Clinical acceptance of computational models depends on rigorous validation against experimental and clinical data, yet achieving such validation is difficult due to variability in patient data, lack of standardized validation protocols, and ethical considerations around data sharing (Pathmanathan & Gray, 2013; Viceconti et al., 2016).

Moreover, current regulatory frameworks for medical technologies are not fully adapted to the complexity of *in silico* models. The use of simulation tools in clinical settings requires compliance with regulatory standards, such as those outlined by the U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA), which are still evolving in their approach to computational modeling and digital twins (Hines et al., 2020; Morrison et al., 2018; Viceconti et al., 2016). These regulations often lack clear guidelines for verifying model credibility, defining acceptable uncertainty margins, or determining conditions under which *in silico* trials can supplement or replace traditional clinical testing. As a result, researchers and developers face difficulties navigating regulatory approval pathways, which can delay or restrict the integration of computational models into routine clinical practice (Erdemir et al., 2020).

Also, the growing use of AI in modeling and clinical decision support brings additional ethical and legal considerations. AI-driven models, particularly those based on machine learning, often operate as "black boxes," offering little transparency in how decisions are made, which raises concerns about trust, interpretability, and accountability (Morley et al., 2020; Topol, 2019). This lack of explainability can impede clinical adoption and conflict with ethical principles in medicine, such as informed consent and clinician responsibility. Additionally, bias in training data, such as underrepresentation of certain demographics can result in uneven outcomes that reinforce health inequalities (Char et al., 2018). Therefore, while computational modeling and AI hold immense potential for transforming heart failure diagnosis and treatment, addressing these technical, regulatory, and ethical limitations is essential for their safe and equitable integration into clinical practice.

3. Materials and Methods

In order to simulate cardiac function, as well as different types of cardiomyopathies (in this specific case the HCM), a geometrically simple parametric model of the left ventricle (LV) is generated, consisting of the base part, the aortic and mitral valves, and the connective part (the junction between the base and the valve; Fig. 1). Each geometric component of the model has a length, diameter, and number of layers (the partition parameter). The fluid domain is bounded by a wall, and the entire model is generated using eight-node finite elements. The elements and nodes of the fluid and solid domains coincide, as a prerequisite for FSI.

Using parametric model of the LV, two different models are generated as shown in Fig. 1, according to the clinical findings. These two models simulate cases of HCM and correspond to patient numbers A and B, respectively. Both patients were under high risk of further HCM progression, while patient A was also under high risk of heart failure. The diagnosis of HCM was established according to the guidelines of the European Society of Cardiology, i.e. HCM is present if the wall thickness is ≥15mm in one or more segments of the left ventricular myocardium (or ≥13mm in individuals with a positive family history of HCM), with abnormal ventricular filling (Elliott et al., 2014) in the absence of any other cardiac or systemic disease that could cause left ventricular hypertrophy, such as valvular heart disease or arterial hypertension. At the time of diagnosis of initial HCM (first examination – initial patient

condition, i.e. *Baseline*), patients underwent a detailed clinical examination. Thereafter, patients underwent regular periodic controls with reassessment of all clinical parameters. Longitudinal data were collected to monitor disease progression. The results of the first (*Baseline*) and last clinical examination (i.e. *Follow up)* have been compared with the results of numerical simulation.

In the parametric model of the LV HCM model, the base diameter is 50.62 mm, the base length is 79.47 mm, the connective length is 10.11 mm, the cross-sectional diameter of the mitral valve is 24.2 mm, the mitral branch length is 18.1 mm, the cross-sectional diameter of the aortic valve is 29.8 mm, the aortic branch length is 18.1 mm, and the wall thickness is 10 mm. The mitral and aortic branches have larger dimensions compared to the real thickness of the aortic and mitral valves in order to prevent possible velocity fluctuations in these zones. Compared to patient A, patient B has a larger LV with thicker walls (15 mm). The given boundary conditions, i.e. the inlet velocity at the mitral valve cross-section and the outlet velocity at the aortic valve cross-section, are shown in Fig. 2. The left ventricular wall is constrained at the top (the upper wall surface, Fig. 1). The nonlinear material model of the heart muscle with fiber orientation is prescribed. The algorithm for automatically generating fibers of appropriate orientation (Bayer et al., 2012) is part of the preprocessing, which, during the computer simulation of cardiac activity, enables the contraction of the heart chambers in a coordinated and efficient manner.

The movement of fluid in the left ventricle can be considered as a laminar flow of incompressible fluid, which is described using the continuity equation and Navier–Stokes equations:

$$-\mu\nabla^2\upsilon_l + \rho\left(\upsilon_l \cdot \nabla\right)\upsilon_l + \nabla p_l = 0 \tag{1}$$

$$\nabla \cdot \upsilon_l = 0 \tag{2}$$

where υ_l is the blood flow velocity, p_l is the pressure, μ is the coefficient of dynamic viscosity of blood, and ρ is the density of blood. These equations can be transformed into the balance equations of a finite element by using the Galerkin method.

The FSI algorithm within the PAK software (*PAK Finite Element Software*, 2025) is used for modeling the LV with nonlinear material model, together with stretches and integration along muscle fibers. Both strong and loose coupling are available in the PAK software, while in this study is performed loose coupling (Filipovic et al., 2006). The domain of the left ventricular wall contained approximately 4000 integration points. The time step used in the FEM simulation is 20 x 0.05 s. The total stress arises from both the contractile forces generated by the muscle and the passive elastic behavior of the surrounding connective tissue and non-contractile structures:

$$\overline{\sigma} = \phi\overline{\sigma}_m + \left(1-\phi\right)\overline{\sigma}^E \tag{3}$$

where ϕ is the fraction of muscle fibers in total muscle volume, $\overline{\sigma}_m$ is the active stress generated in muscles and $\overline{\sigma}^E$ is the stress in the passive part of the muscle. The Holzapfel material model (Holzapfel & Ogden, 2009; McEvoy et al., 2018) is implemented to calculate the passive stresses within the wall, while the MP surrogate model (Prodanovic et al., 2021) is used to calculate the active stresses, including input MP parameters generated and fitted using implemented algorithms (Mijailovich, Prodanovic, Poggesi, Geeves, et al., 2021).

For calculating active stresses, it is also possible to implement the Huxley model (Huxley, 1957), however, the calculation is very computationally and time-consuming. The procedure required for performing the calculation is following:

1. Input data – applied calcium concentration, LV geometry including muscle fiber orientation, inlet and outlet velocities, material characteristics, input parameters for MP solver;
2. Data processing and computation – coupling of FSI solver and MP model;
3. Output data – results of simulations including files with different mechanical parameters (velocities, pressures, stresses, displacements, etc.).

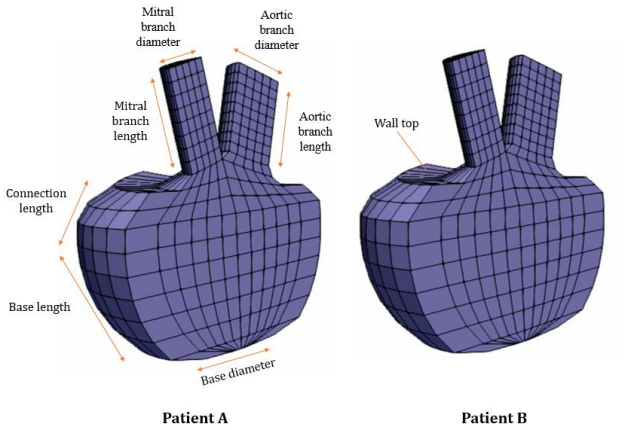

Fig. 1. Parametric 3D models of HCM LV with specific parametric parts: base part, valves (aortic and mitral) and connecting part (connection between base and valves).

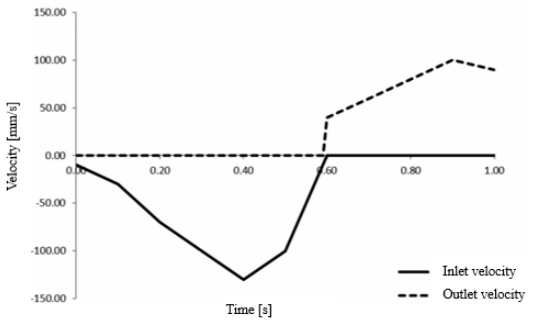

Fig. 2. Prescribed inlet and outlet velocities in the mitral and aortic valves, respectively.

4. Results and Discussion

Patients A and B with clinically diagnosed HCM and under high risk of severe clinical events (progression of HCM for both patients, potential heart failure for patient A), have been analyzed in the PAK software, simulating the cardiac cycles and analyzing the resulting biomechanical parameters (Tomasevic et al., 2023). The left ventricular geometries for patients A and B are shown in Fig. 1, respectively. It should be emphasized that the parametric geometric models are simplified and generated based on dimensions measured on specific patients, i.e. geometric

parameters are obtained based on specific patient data (Filipovic, Sustersic, et al., 2022). Also, the measured valve diameters and heart wall thicknesses are used to generate the finite element mesh of the parametric left ventricular model. The lengths of the mitral and aortic branches do not affect the calculation results. Nominal values of inlet and outlet velocities have been adopted (Fig. 2), and then scaled according to the valve diameters. The inlet velocity is proportional to the mitral valve diameter, while the outlet velocity is proportional to the aortic valve diameter.

The PAK software results obtained for patient A show the distribution of displacements, pressures, and velocities, respectively (Fig. 3). Since the injection part of the cardiac cycle occurs during the first few steps of the simulation, displacements are noticeable at the mitral valve and in the base part of the model. At the moment of contraction and pumping blood from the left ventricle (t = 0.7 s), the lower half of the wall suffers the greatest deformation. During the remaining simulation time, the wall gradually returns to its original state (t = 1.0 s), while the deformations decrease.

During diastole, i.e. during the first part of the cycle, blood is pumped into the left ventricle, increasing its volume, while the pressure is maximal at the mitral valve (t = 0.4 s). When the injection cycle is complete and the mitral valve is closed, the ventricle contracts and pumps blood through the aortic valve, resulting in maximal pressure. Velocities in the left ventricle are maximal during systole (t = 0.4 s) when blood accelerates and is pumped through the aortic valve. At the moment of blood injection into the left ventricle, velocities are greatest in the mitral valve region (t = 0.1 s).

The displacements, pressures, and velocity fields for patient B are shown in Fig. 4. The displacements are greatest in mid-diastole during pumping of blood into the ventricle. Near the end of the cardiac cycle, the left ventricular model returns to its initial configuration.

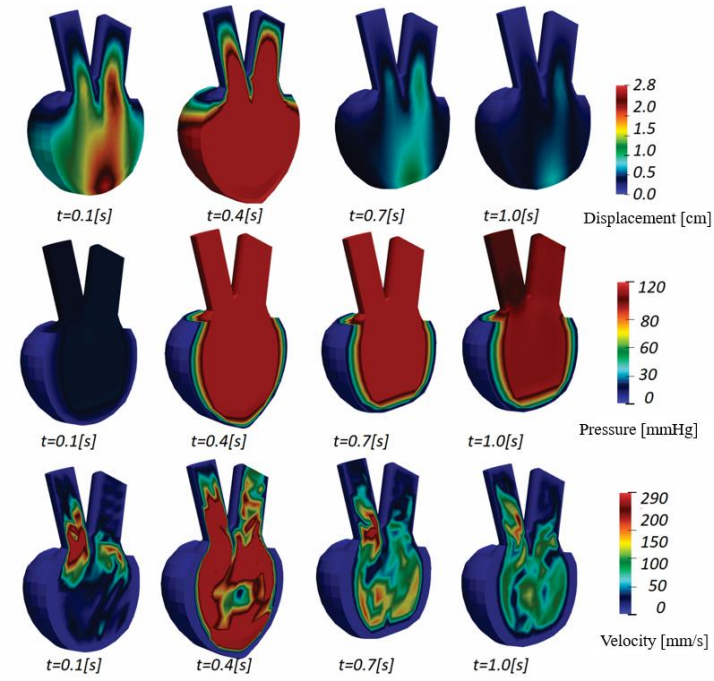

Fig. 3. HCM LV model for patient A – Displacements, pressures, and velocity fields during the cardiac cycle, respectively (Tomasevic et al., 2023).

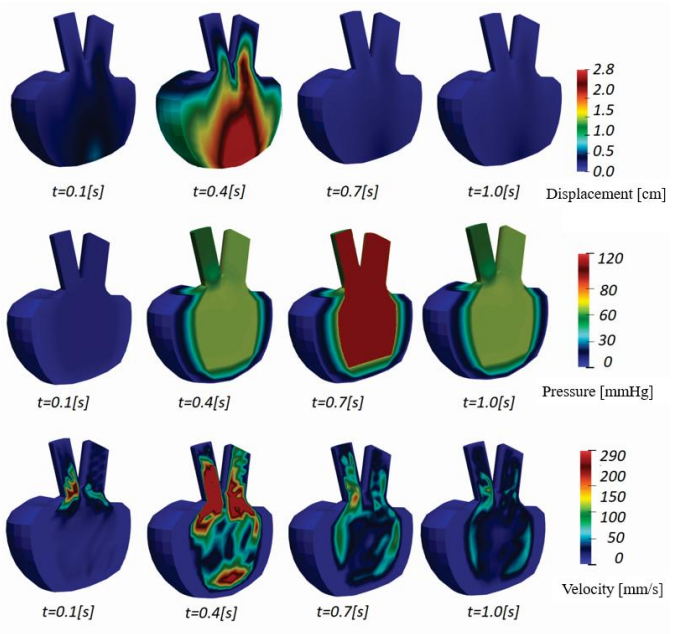

Fig. 4. HCM LV model for patient B – Displacements, pressures, and velocity fields during the cardiac cycle, respectively (Tomasevic et al., 2023).

In addition, as a result of the simulations in the PAK software, the Pressure-Volume (PV) diagrams for patients A and B are also presented (Fig. 5). The PV diagrams are graphical representations of the relationship between pressure and volume in the left ventricle during the cardiac cycle. These loops provide detailed insight into the mechanical function of the heart, allowing clinicians and researchers to evaluate key parameters such as stroke volume, End-Diastolic Volume (EDS) and End-Systolic Volume (ESV), and ventricular contractility. In the context of heart failure, PV diagrams are especially valuable for identifying impaired ventricular function, reduced Left Ventricular Ejection Fraction (LVEF), and altered pressure dynamics, all of which are crucial for diagnosing HF severity and monitoring therapeutic outcomes (Bastos et al., 2020).

In case of obtained results, the pressure change is similar in both patients, while patient B has a larger volume change in the simulated *Follow up* state compared to patient A. The health condition of patient A has worsened; therefore, the simulated *Follow up* state shows a reduced volume change between end-diastole and end-systole in the PV diagram.

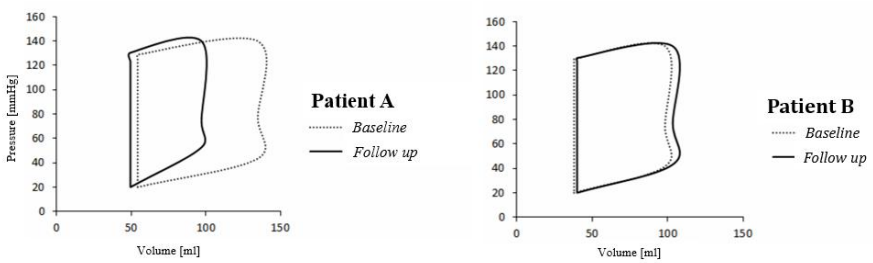

Fig. 5. Change of PV diagrams at simulated *Baseline* and *Follow up* states, for patients A and B, respectively (Tomasevic et al., 2023).

The results for *Baseline* and *Follow up* states are consistent with the clinical observations. Namely, the clinically measured and computationally obtained values of LVEF are compared for patients A and B at *Baseline* and *Follow up* states, presenting good correlation. The LVEF is calculated as LVEF = (EDV − ESV)/EDV (Djorovic, 2022). The clinically measured LVEF for patient A is 64% at *Baseline* and 50% at *Follow up*, while computationally obtained LVEF is 59.75% at Baseline and 49.1% at *Follow up*. Additionally, the clinically measured LVEF for patient B is 60% at *Baseline* and 60% at *Follow up*, while computationally obtained LVEF is 61.42% at Baseline and 61.4% at *Follow up*. It can be concluded that the simulated LVEF in the *Follow up* state remains almost unchanged for patient B, but it is reduced for patient A whose actual health condition was worse, leading to potential heart failure (Tomasevic et al., 2023).

In clinical practice, LVEF is a useful parameter for assessing the patient's condition, however, cardiologists need additional information for accurate diagnosis, considering that LVEF can be normal or even high, and the left ventricle does not pump a sufficient amount of blood at the same time (Maron et al., 2018). For this purpose, the results and developed methods from *in silico* clinical studies can be applied, contributing to improving risk assessment and the direction of therapy for specific patients.

5. Conclusions

This study includes an overview of related work in the field of cardiomyopathies and heart failure, covering computational modeling, FEA and AI, the use of medical data for model development and validation, as well as existing platforms and models in cardiomyopathy and heart failure research, highlighting current gaps and opportunities for innovation. More importantly, it demonstrates the potential of computational modeling to provide deeper insights into the biomechanical and functional changes associated with HCM and its progression toward heart failure. By using the PAK software to simulate cardiac cycles in two patients with clinically diagnosed HCM, we are able to analyze key parameters such as pressure, velocity, displacement, and pressure-volume (PV) relationships. The comparison between computational simulations and clinical data show strong agreement, particularly in the evaluation of LVEF, supporting the validity of the modeling approach.

The results highlight the value of computational tools in complementing clinical findings, enabling a non-invasive, patient-specific analysis of cardiac mechanics that can track disease progression over time. By replicating both *Baseline* and *Follow up* conditions, the model proved useful in evaluating how structural and functional changes manifest across different stages of HCM, with implications for earlier detection and more tailored therapeutic interventions. Moreover, the continuous development of the PAK software and its evolving capabilities for multiscale simulation are critical for expanding its applications in cardiovascular research. Enhancing its integration with clinical data and other computational platforms will further increase its potential as a powerful tool for both research and clinical decision support.

In summary, the application of computational modeling in the study of cardiomyopathies and heart failure is an exciting and rapidly evolving field. The integration of multiscale modeling, together with finite element analysis, offers valuable tools for improving diagnosis, treatment, and outcome prediction. The incorporation of patient-specific data further enhances model accuracy, making personalized medicine a reality in the treatment of heart disease. However, challenges such as data integration, model generalization, and computational cost remain. As these challenges are addressed, computational models will likely play an increasingly important role in improving the management of heart failure and related cardiomyopathies.

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