Description of the aims and objectives

The project proposes the development of research activities of both experimental and theoretical nature aimed to the measurements, analysis and study of heart’s vortices for the prediction of heart failure (HF).

The final objective of this research project will be to define a predictive model, based on the properties of vortices created by the blood flow in the heart chambers, which allows the early prediction of ventricular remodelling and HF. The proposed activities will have a total duration of three years during which a thorough study of the vortex motions will be conducted for creating a mathematical model based on clinical data capable of improving the early assessment of the failure of cardiac function. The model is aimed to the prediction of left ventricle (LV) remodelling by providing physically-based, clinically-tested guidelines useful as a conceptual ground to future clinical research which is demonstrating great relevance arousing the study of cardiac fluid dynamics.

State of the art

HF is the principal threat of cardiac progressive dysfunction. It presents both as a primary dysfunction or as consequence of other dysfunctions or following therapeutic interventions. Despite the recent clinical progress the mortality rate is high, in fact over 50% of patients with diagnosis of HF die within five years (Levy et al. 2002).

The physiological causes that lead to remodelling of LV are mainly attributed to an increase of the stress on the myocardial fibers that stimulate the growth and multiplication of cells and give rise at an increase of muscle thickness, and then the dilatation (Sengupta and Narula 2008). The current models of cardiac remodelling are not predictive and, in particular, do not take into account of the blood motion inside the heart that can participate to the sequence of events that lead to the progressive remodelling of the LV and finally to HF (Pasipoularides 2012; Pedrizzetti et. al 2015). The peculiarity of cardiac fluid dynamics is the presence of high accelerations, and thus forces, due to rapid changes in the direction and intensity of the blood velocity (Pedrizzetti et al. 2015). In the recent years, numerous studies on the dynamics of vortices into the LV have been conducted using different techniques among which: numerical simulations, MRI, echocardiography (Markl et al. 2011). Despite all these studies have shown the presence of a relationship between the cardiac function and the quality of the intraventricular fluid dynamics (Mangual et al. 2013), there is as yet no complete mathematical model capable to predict the onset of HF. This is partly imputable to the absence of repeatability and reproducibility of the measurements able to characterize these vortex motions and define the complex transduction mechanism (Pasipoularides 2012).

References

Levy D, Kenchaiah S, Larson MG, Benjamin EJ, Kupka MJ, Ho KKL, Murabito JM, Vasan RS.

This proposed project aims to measure, define, analyze and reconstruct the vortex flows in both healthy and pathological subjects in order to be able to characterize regularities and anomalies, and so consequently to predict in advance the onset of HF. For the study of ventricular pressure is possible to start from Laplace law. This describes the relationship between the transmural pressure, the tension of the LV membrane wall at a point and the entity of the curvature of the wall at that point. The characteristics of LV to take in consideration for this study are: Preload and Afterload. Preload is the hemodynamic load on the ventricular wall at the end of diastole while the Afterload is the load imposed at ventricle during ejection. The physical properties of the blood are known, while its motion obeys the mathematical laws governing the mechanics of fluids: conservation of mass (continuity equation) and conservation of momentum (Navier–Stokes equation) whose solution can be performed by numerical techniques which are called direct numerical simulations (DNS) (Mangual et al. 2013). Numerical simulations of the blood motion inside the LV and the fluid-tissue interactions models to date are still not well represented because different choices of calculating show different advantages and disadvantages, nevertheless, recent progress allow to start drawing a unified framework on the mechanics of LV fluid in normal condition and annexed its variations in presence of pathologies. Computational fluid dynamics is the primary tool for a detailed understanding of the physical phenomena that participate at flow of LV. However, this must be completed by real “in vivo” measurements, performed by imaging technologies, which represents a complementary approach necessary to correlate the theoretical studies with their clinical relevance (Pedrizzetti and Domenichini 2014).

The latest imaging technologies and their integration with computational methods allow visualization and quantification of the fluid dynamics of LV. The present project is expected to develop a scientific collaboration with a clinical cardiologic centres. In this way it will be possible to analyse and verify the data from a certain number of patients in order to demonstrate the reproducibility and reliability of the technique.

Blood flow in the LV will reconstructed by DNS through the calculation of the intraventricular blood motion corresponding to the LV moving geometry and properties of the inlet/outlet orifices (Mangual et al. 2013). The numerical solution technique utilizes the Immersed Boundary (IB) method which allow an immediate integration with medical imaging and is capable to manage with relative ease the wide motion, up to closure, of cardiac valves. In this approach the LV geometry segmented from medical imaging is immersed inside the computational domain and the inflow/outflow follow automatically by mass conservation ensured from the system of equations. LV fluid dynamic is evaluated by several metrics selected to quantify the flow properties: Vortex Formation Time, Kinetic Energy Dissipation and Flow Transit. This gives a blood transit curve that measures the percentage of Stroke Volume (SV) that has been ejected after a number of heartbeats. We will also compute the properties that characterize the dynamic fluid-tissue interaction between blood flow and LV:
pressure gradient and wall shear stress. These are expected to be the relevant in the development of LV remodelling like they are for the development of embryonic heart (Pedrizzetti et al. 2015). For evaluating the intraventricular flow by DNS is necessary an input from echocardiographic or cardiovascular magnetic resonance (CMR) clinical imaging to bound the flow domain, then DNS provides an evaluation of LV flow with high spatial resolution. For this study, in order to obtain more detailed data will be used most advanced techniques of imaging analysis: 4D echocardiography or 4D CMR (Lai et al. 2014). First simulations are made on ideal cases to compare with existing results and general clinical information. Subsequently, simulations will be made on real data obtained from clinical structure for comparing with corresponding flow information obtained from imaging data. The information obtained from DNS will be evaluated with respect to the follow-up of patients to evaluate which information is more predictive for clinical progression. The objective is to create a functional DNS model aligned with real data of patient in order to determine a useful model for predicting HF. Moreover, this method is non-invasive and is a great incentive for the study of the cardiac fluid dynamics.

References


Scheduling

The first year will be dedicated to study and become operative with techniques of to blood flow reconstruction through DNS, and with cardiovascular imaging tools.

The second year will be dedicated to validation, developments and comparison of numerical simulations results with clinical information and with corresponding data from images in order to characterize the flow properties with clinical pathology.

During the third year, numerical simulations are performed systematically on groups of real patients data obtained from clinical structures. The objective is to create a functional DNS model aligned with real data of patient in order to determine a useful model for predicting HF.

Roma, 07/09/2016

Signature