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Intraventricular flow features and cardiac mechano-energetics after mitral valve interventions – feasibility of an isolated heart model

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Abstract: The aim of this work was the development of an isolated heart setup to delineate the interactions between intraventricular flow features, hemodynamic parameters and mechano-energetics after certain mitral valve therapies. Five porcine hearts were explanted and prepared for (i) edge-to-edge mitral valve repair, (ii) implantation of a rotatable biscupid mechanical valve prosthesis. Flow structures were visualized using echocardiography while hemodynamics was recorded in terms of pressures, flow rates and ventricular volume. Hemodynamic and cardiac mechano-energetics implied a marginal effect (<5%) of alternating leaflet orientation on ventricular pre-load and stroke work. After edge-to-edge repair, substantial variations in flow structures were observed. Beside promoting profound insights into fundamental physiologic mechanisms, the setup may be used for validation of computer aided therapy planning tools.

Keywords: *ex-vivo*; isolated heart; mechano-energetics; MitraClip®; mitral valve intervention; mitral valve prosthesis; 3R; ventricular flow.

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Introduction

Mitral valve interventions primarily aim at restoring valvular function to treat insufficiency or stenosis. In contrast, secondary objectives such as preserving and regaining optimal intraventricular flow structures for ventricular washout and efficient cardiac function remain poorly understood and could soon be considered in computer assisted therapy planning tools. However, comprehensive data delineating the effect of mitral valve interventions on intraventricular flow fields and cardiac mechano-energetics is missing and hamper both development and training of elaborate therapy planning algorithms. Existing studies provide even controversial results regarding the impact of the intraventricular flow structures on cardiac mechano-energetics and hemodynamic characteristics. While several studies report a strong influence of vortex patterns [1, 2] and energy dissipation of up to 15% caused by changing left ventricular (LV) flow patterns, [3] others contradict this theory and claim no substantial influence [4, 5].

Hereby motivated, the aim of this study was to establish an isolated beating porcine heart setup which permits the investigation of the complex relationship between flow structures, hemodynamic parameters and cardiac mechano-energetics under defined conditions following selected mitral valve interventions. This setup may not only contribute to fundamental insights into post-interventional cardiac physiology, but also function as a validation tool for numerical methods [6], approaching the need for improved therapy planning support.

Materials and methods

Isolated heart setup

An isolated heart setup was employed as previously proposed [7, 8] and adapted to the distinct needs of this study. Hearts of five pigs

(40–75 kg) were explanted before termination of concomitant acute animal experiments according to the protocol described by Granegger et al. [9] and in line with the 3R strategy. On three hearts, a surgical edge-to-edge mitral valve repair was performed to mimic the implantation of a MitraClip® device (Abbot Vascular, Inc., Santa Clara, California) (Figure 1a). In two hearts, a bicuspid mechanical mitral valve prosthesis (Open PivotTM, 25 mm; Medtronic, Ireland) was implanted, modified to enable leaflet rotation (0–90°) during the experiments (Figure 1b). After connection to the experimental setup, the organ was reanimated in the Langendorff modus [8]. Once the heart beat stabilized, the setup was switched to the working mode with the left heart pumping blood from the left atrium towards the aorta.

Left atrial and aortic pressure were continuously measured by APT300 pressure sensors (Hugo Sachs Elektronik – Harvard Apparatus GmbH, Germany), while arterial and coronary flow were monitored using Sonoflow CO.55/120 V2.0 sensors (SONOTEC GmbH, Germany). Pressure-volume loops of the left ventricle were derived from catheter based measurements (VentriCath 510, ADinstruments, New Zealand) of intraventricular pressure and volume.

Study protocol

Hemodynamic measurements were recorded during both native and clipped mitral valve condition (Figure 1a) while the heart was beating in a stable working mode. In the hearts implanted with the mechanical valve prosthesis (Figure 1b), hemodynamic measurements were taken with the valve implant oriented in the anatomical position (anterior and posterior leaflet configuration), as well as in an anti-anatomical leaflet position (leaflet rotation $\varphi \simeq 90^{\circ}$, see Figure 2). Cardiac output and heart rate were kept constant for both prosthesis orientations. The respective valve position was maintained for 1 min after rotation and mechano-energetic parameters were taken before switching to the other position. This procedure was repeated four times per measurement series. The percentage change in hemodynamic and cardiac mechano-energetic parameters was determined between baseline condition (anatomical position) and its corresponding anti-anatomical position. The Wilcoxon signed-rank test with Bonferroni correction for multiple testing was employed to determine statistical significance of these changes (p-value<0.05).

Image acquisition and processing

For all mitral valve configurations, echocardiographic B-mode images were acquired with frame rates of 150-200 per second in the Hyper 2D mode of an EPIQ7 Ultrasound System using a X5 probe (Philips Healthcare, Netherlands). Recordings were taken for 10 s after the injection of contrast-enhancing micro bubbles. The bubbles were generated in 5–10 mL saline water-air solution (9:1) that was reciprocated in five successive, firm agitations between two connected syringes [7].

Ultrasound particle image velocimetry (PIV), also known as Echo-PIV was used for flow field analysis. Aiming at feature and contrast enhancement, the DICOM images were pre-processed using a snapshot POD (proper orthogonal decomposition) and high mode reconstruction to suppress tissue motion and obtain improved contrast of the tracer bubbles. An iterative PIV algorithm [10] was used to quantify the intraventricular flow patterns. In contrast to previous approaches, time averaging over several heart beats [7] was replaced by a time-resolved PIV evaluation. Subsequent post-processing on the velocity field was applied to identify predominant flow structures and allows data processing also in case of cardiac arrhythmia.

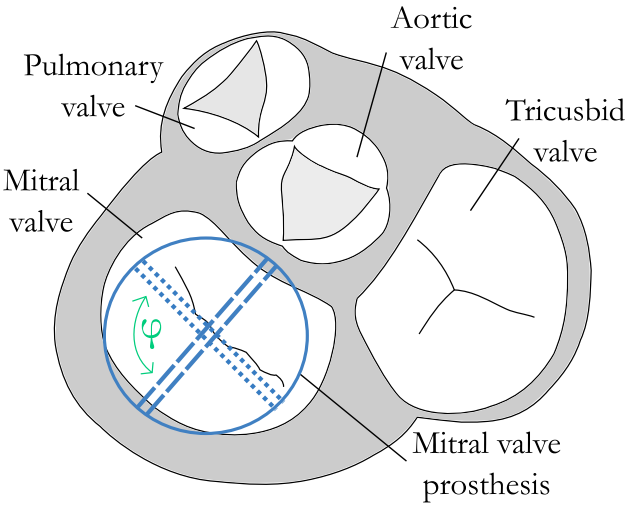

Figure 2: Valvular plane with schematic orientation of the mechanical mitral valve prosthesis in anatomical (dotted) and anti-anatomical (dashed) position.

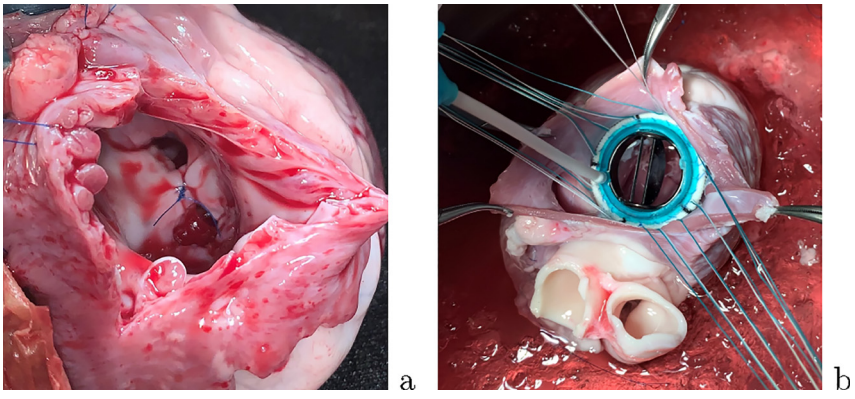

Figure 1: a) View on the stitched and connected mitral valve leaflets through the left atrium. b) Implantation of rotatable bicuspid mitral valve prosthesis.

Results

Intraventricular flow

Flow field evaluations are shown for (i) the native valve condition at a heart rate of 53 bpm with a cardiac output of 27 mL and (ii) for a clipped valve condition at a heart rate of 87 bpm and 31 mL cardiac output (Figure 3). In the native valve condition, the flow structures appeared with the expected pattern of a large clockwise rotating vortex during diastole and an outflow jet directed straight towards the aorta during systole (Figure 3a, b) [1, 7]. Preliminary results showed a considerable effect of the clipped valve and the resulting double orifice on the ventricular flow structures. In a three chamber view, the two jets emerging through the respective orifices were not distinguishable in the early diastole. The visible inflow jet showed the tendency to point more towards the septum than the jet emerging through a native valve. Two counter-rotating vortices developed during mid-diastole and persisted until late diastole (Figure 3c). Systolic flow patterns indicate that small counter-rotating vortices remain in the area of the apex (Figure 3d).

Cardiac mechano-energetics

A total of eight measurements of cardiac mechano-energetics were performed in two hearts. Heart rate, mean arterial pressure and cardiac output did not change considerably (median less than 0.5%) when the mechanical valve was rotated from anatomical to anti-anatomical position (Figure 4). A trend towards a decrease in left atrial pressure and external work was observed with the valve in anti-anatomical position at a median drop of −4.2% and −2.2%, respectively (Figure 4). However, these changes were not statistically significant.

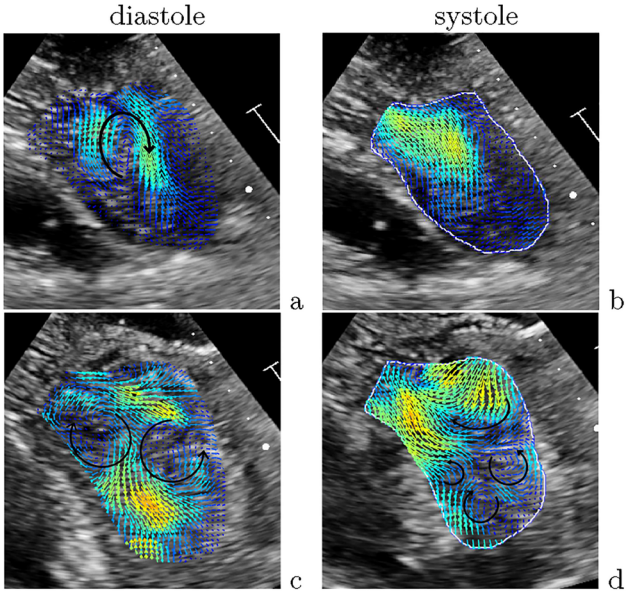

Figure 3: Echo-PIV evaluation of LV flow with native valve during a) diastole, b) systole; after edge-to-edge repair during, c) late diastole and d) late systole.

Discussion

In this study, an isolated porcine heart model was developed to delineate interactions between intraventricular flow structures, hemodynamic parameters and mechano-energetics after selected mitral valve therapies. The effect of both edge-to-edge repair and mitral valve prosthesis orientation was previously investigated mainly in numerical and experimental studies [2, 11], while few *in vivo* studies [1, 12] exist on these topics. This is the first time an *ex vivo* experiment under physiological conditions has been employed for equivalent research purposes.

Intraventricular flow

The flow data evaluated in this study showed discrepancies in intraventricular vortex patterns over the entire heart beat after an edge-to-edge procedure on the mitral valve. Even though the preliminary results of this study point in a similar direction predicted in simulation studies, further experiments are to be undertaken to confirm these

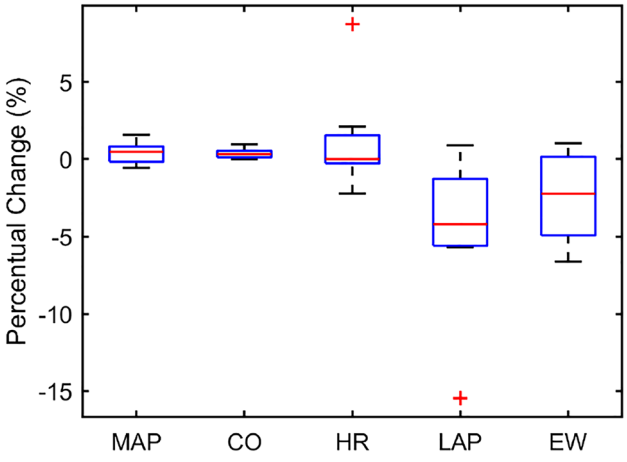

Figure 4: Percentual changes in hemodynamic and cardiac mechano-energetic at a rotation of the mechanical valve from anatomical to anti-anatiomical position. MAP – mean arterial pressure; CO – cardiac output; HR – heart rate; LAP – left atrial pressure; EW – external work.

findings. Beside promoting the identification of flow structures, the approach could perspectively be used to gain more information about vortex structure related residence time and cardiac washout. These parameters are often linked to thrombo-embolic events and cardiac energetics [2].

Cardiac mechano-energetics

A slight trend towards a drop in left atrial pressure and external work is indicated by first results obtained with the mechanical valve in anti-anatomical position at constant cardiac output, heart rate and mean arterial pressure. Whereas these results point towards a slightly improved ventricular function with an anti-anatomical valve position, further experiments are required to validate the results and delineate the causality of the observed changes. Even though other factors might be affecting the results, it may be hypothesized that the flow field with the mechanical valve in the anti-anatomical position [2] leads to energetically beneficial conditions for ventricular performance.

Preliminary data indicate the potential of the isolated heart setup to provide insights into the effect of mitral interventions on intraventricular flow patterns and cardiac mechano-energetics under controlled and physiological conditions. The results regarding the possible interaction between ventricular flow fields and mechano-energetics substantiate further studies to delineate the underlying mechanisms. Eventually, the isolated heart setup may contribute to the development and validation of computer assisted therapy planning tools [6].

Limitations

The study is restricted to five isolated porcine hearts. Even though the feasibility of the respective methodology was shown, the data does not suffice for broad statistical analysis. Due to the reuse aspect of the 3R approach, the animals may have conceived medication that impacts on the heart performance.

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