Left Atrium Hemodynamic in Atrial Fibrillation and Normal Subjects

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Abstract

Atrial Fibrillation (AF) is associated with a five-fold increase in the risk of cerebrovascular events. Recent studies suggest that a computational fluid-dynamics (CFD) approach could provide insights on AF mechanisms thus potentially allowing a quantitative assessment of cardioembolic risk. The goal of this study was to use a previously developed patient specific CFD model of the left atrium (LA) to enhance differences in blood flow in AF patients and normal subjects. In this study we computed left atrium blood flow and derived parameters in normal subjects (NL), patients affected by paroxysmal AF (PAR-AF) and patients affected by persistent AF (PER-AF). Results showed mean peak velocities continuously decreasing from NL to PER-AF groups. In agreement, a lower number of vortex structures was observed in PER-AF with respect to PAR-AF and NL, thus limiting an effective washout of the LA and the left atrial appendage (LAA). Velocities at the LAA ostium and inside the LAA were also strongly reduced showing a limited washout effect as confirmed by blood stasis in terms of number of particles still present after five cardiac cycles within the LAA (NL: 5±2, PAR-AF: 18±3, PER-AF: 41±10). The developed approach quantifies differences in LA hemodynamic in AF and NL subjects, also allowing a stratification of the disease progression in terms of changes in the blood velocity, organization of blood flow and quantification of blood stasis.

1. Background

Atrial Fibrillation (AF) is the most common form of arrhythmia worldwide. In 2010, the estimated number of persons with AF worldwide exceeded 31 million, with higher incidence and prevalence rates in developed countries [1]. These numbers are expected to double in the next 50 years as the population mean age increases [2]; in addition, very recent studies reported an increase of more than 30% in AF episodes in states with higher COVID-19 prevalence suggesting a possible association between pandemic-associated social disruptions and AF [3].

Such scenario enables to also predict a significant increase in the risk of cerebrovascular events [4], being nowadays AF responsible of 15-18% of all strokes. The formation of clots is favored by the electro-anatomical remodeling of the atria subject to AF: modifications of the electrophysiological and structural characteristics of the myocardium which gradually become thicker in correlation with the duration of the arrhythmia, might affect left atrium (LA) contraction and consequently increase blood stasis and thrombus formation. Unfortunately, such parameters are not available in clinical practice and the most used index for the assessment of stroke risk is the CHA_2DS_2-VASc based on the most common clinical stroke risk factors/modifiers [5].

In this study we hypothesized that stroke risk stratification in AF patients could be improved by using information on blood flows within the LA and left atrial appendage (LAA) [6]. To test this hypothesis, we applied a previously developed computational fluid dynamics (CFD) model [7] to enhance the differences in blood flow in AF patients and NL. The most important parameters from the CFD model that potentially stratify the stroke risk were computed and evaluated to better understand the relationship between AF progression and stroke risk on a patient-specific basis.

2. Methods

2.1 Patient data

The study was performed in collaboration with the Bioengineering group of the University of Bologna and the Department of Cardiology and Radiology of AUSL Romagna, Santa Maria delle Croci Hospital in Ravenna, Italy. The F.A.T.A. (Fluid-dynamics in the left Atrium in atrial fibrillation patients and in controls for Thrombogenic risk Analysis) study was approved by the Romagna Ethical Committee (Prot. 1276/2019 I.5/6).

F.A.T.A. study includes 100 patients; we already enrolled 19 subjects: 10 normal subjects (NL), 5 patients affected by paroxysmal AF (PAR-AF) and 4 patients affected by persistent AF (PER-AF).

CT data of the LA were acquired in sinus rhythm from a Philips Brilliance 64 CT scanner. Ten volumes (170 axial slices, 0.4 mm pixel size, 1 mm slice thickness), covering a cardiac cycle from the end of ventricular diastole, were reconstructed by retrospective ECG gating and used for the following analysis described in the next subsection.

Doppler data were acquired at the MV and PVs. Unfortunately, only in one patient belonging to the control group, the MV Doppler was available; in the other subjects Doppler data were not acquired and

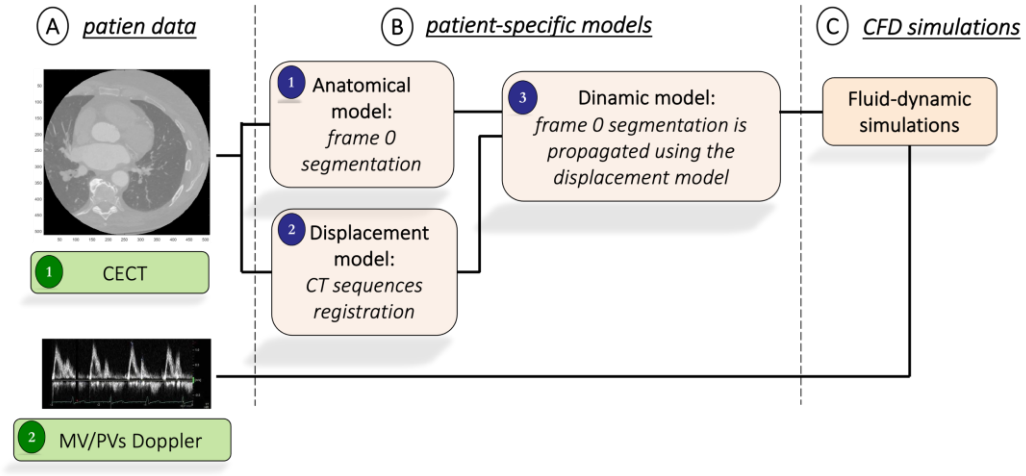

Figure 1. The workflow of the F.A.T.A. study: patient-specific contrast enhanced CT (CECT) data (A1) are processed to derive the LA anatomical and displacement models (B1-2) from which a dynamic mesh (B3) is computed; together with the Doppler measurements (A2), this dynamic mesh represents the computational domain for the personalized CFD model (C).

were derived from literature, representative of both NL and AF patients.

2.2 Data analysis

The workflow we developed for data processing is shown in Figure 1. For additional details regarding the CFD model, readers should refer to [7].

In this study, for the definition of the patient-specific LA motion and anatomical models, we applied the same methods and procedures described in [7]. We were able to reconstruct the patient-specific LA geometry and its displacement model throughout the cardiac cycle for NL and AF patients. The series of dynamic meshes represented the computational domain for the simulation.

Simulations were performed in sinus rhythm condition. Each simulation was performed for five cardiac cycles in order to reduce the influence of the initial conditions on the outputs. For each model, the blood velocity field, the vortex structures and kinetic energy were analyzed for both LA and LAA. In addition, the blood stasis within the LAA was evaluated. In particular, blood stasis was assessed by populating the LAA with 500 particles and counting the number of particles still present after five cardiac cycles.

For the parameters of the CFD model, the time step was set at 0.01 seconds, the dynamic viscosity at 0.035 poise and the density at 1.06 g/cm^3.

The CFD simulations were performed through the LifeV library [8].

3. Results

Data processing and simulations were feasible in all study subjects.

Velocities inside the LA and in the LAA had different amplitude and distribution in the three groups. We found higher values of the velocity inside the LA and in the LAA in the control group with respect to the AF patients. In Figure 2, we show the velocity field inside the LA in one representative subject for each group. During left ventricular (LV) systole, MV velocity was zero, as expected. However, we can notice an increase in speed in correspondence of the PVs during LV systole (Figure 2, 1st row) due to the atrial diastole (peak velocity – NL: 55 cm/s, PAR-AF: 40 cm/s, PER-AF: 15÷20 cm/s). At the beginning of the LV diastole (Figure 2, 2nd row) we noticed an increase in speed at the MV, especially for the NL (peak velocity – NL: 95 cm/s, PAR-AF: 80 cm/s, PER-AF: 60 cm/s), due to the MV opening. With regard to the atrial systole (Figure 2, 3rd row), we found a significant reduction in the MV flow speed of AF patients, particularly in the PER-AF (peak velocity – NL: 50 cm/s, PAR-AF: 35 cm/s, PER-AF: 25 cm/s), probably due to the reduction of the LA contractile activity. Considering the average values for all patients in each group, the velocity field presented different amplitude and distribution (peak velocity – NL: 50÷60 cm/s, PAR-AF: 40÷50 cm/s, PER-AF: 15÷25 cm/s). Such differences in velocities are probably due to a stronger contraction-expansion of the LA throughout the cardiac cycle in NL with respect to the AF patients, in which the arrhythmia probably caused a reduction of the contractile activity of the LA cells. In AF patients, we also detected a non-perfect synchronized contractile activity with a less organized blood flow pattern within the LA chamber compared to the control patients.

The mean velocity at the ostium of the LAA and inside the LAA was also decreasing from PAR-AF to

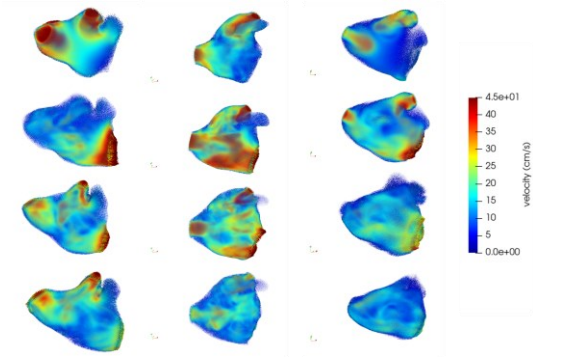

Figure 2. LA velocity field in 3 representative subjects (NL, PAR-AF and PER-AF in the 1st, 2nd and 3rd column respectively), in four phases of the cardiac cycle (1st row: beginning of ventricular systole, 2nd row: beginning of ventricular diastole, 3rd row: atrial systole and 4th row: end of the ventricular systole).

PER-AF (mean velocity – PAR-AF: 25÷35cm/s, PER-AF: 8÷20cm/s) strongly reducing the wash-out effect. In Figure 3 we show the velocity field within the LAA for the same patients reported in Figure 2. Higher values of LAA ostium velocity and of peak velocity were observed at all time points of the cardiac cycle for NL compared to AF patients, which allowed for better LAA washout and less probability of blood stasis.

Moreover, other parameters as kinetic energy showed much higher values in healthy patients with respect to the AF patients, confirming the results previously reported for blood velocity.

The number of the vortex structures and their dimension was much higher in NL with respect to the AF patients in all the time instants of the cardiac cycle. Moreover, the vortex structures covered all the LA (Figure 4, 1st column). This behavior ensured a strong washout within the LA chamber, therefore the risk of blood statis could be considered as null. Regarding the AF simulations, we observed that the number and the dimension of the vortex structures was higher in the PAR-AF patient with respect to the PER-AF patient. These findings confirmed that the contractile activity of the LA in the AF paroxysmal patient was not compromised as for the persistent AF case. The presence of higher number of vortex structures with respect to the PER-AF allowed a better washout within the LA and could reduce the probability of the blood stasis. Moreover, during the E and A wave (Figure 4, 2nd and 3rd row), most of the vortex structures converged to the MV with high velocities in the control group in which the blood flow was more organized with respect to the AF patient where the blood flow resulted more chaotic. To this purpose, a ring shape structure around the MV was observed in the AF patients during the ventricular diastole and atrial systole, bigger in the persistent AF patient. This vortex structure meant that the blood flow also rotated around the MV before

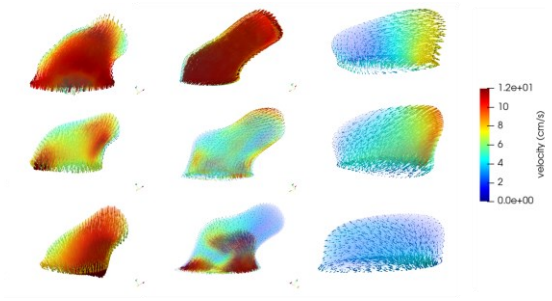

Figure 3. LAA velocity field in 3 representative subjects (NL, PAR-AF and PER-AF in the 1st, 2nd and 3rd column respectively), in three phases of the cardiac cycle (1st row: ventricular systole, 2nd row: ventricular diastole, 3rd row: atrial systole).

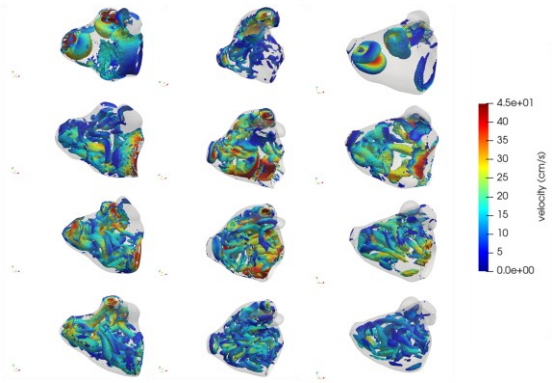

Figure 4. LA vortex structures in 3 representative subjects (NL, PAR-AF and PER-AF in the 1st, 2nd and 3rd column respectively), in four phases of the cardiac cycle (1st row: beginning of ventricular systole, 2nd row: beginning of ventricular diastole, 3rd row: atrial systole and 4th row: end of the ventricular systole).

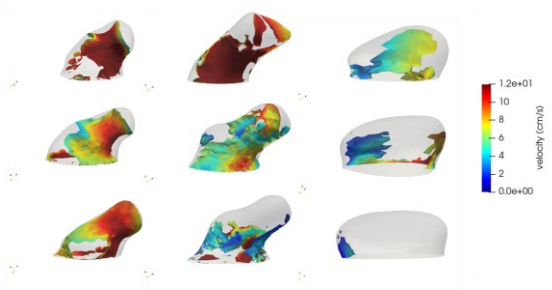

Figure 5. LAA vortex structures in 3 representative subjects (NL, PAR-AF and PER-AF in the 1st, 2nd and 3rd column respectively), in three phases of the cardiac cycle (1st row: ventricular systole, 2nd row: ventricular diastole, 3rd row: atrial systole).

passing to the LV, implying a less direct blood flow pattern in correspondence of E and A wave.

From Figure 4 we also clearly observed that the LA volume variation (contraction/expansion of the LA chamber) throughout the cardiac cycle was higher in the control case with respect to the AF patients. Moreover, in the paroxysmal AF patient, LA volume variation was higher than in the persistent AF patient, especially the LA contraction during and after the atrial systole (Figure 4, 3rd and 4th row). Indeed, we noticed that the volume variation of the LA for the AF persistent case was strongly reduced, and this could favor the risk of blood stasis. The presence of the LA motion throughout the cardiac cycle fosters the vortex structures to leave the LA chamber and to guarantee the blood washout within the LA chamber. Analysis of vortex structures in the LAA substantially confirmed what was already seen analyzing the velocity distribution within the LAA (Figure 5).

The fluid particle analysis in the LAA confirmed these results (NL: 5±2, PAR-AF: 18±3, PER-AF: 41±10).

4. Discussion and conclusion

The developed approach quantifies differences in LA hemodynamic between AF and NL, also allowing a stratification of the disease progression in terms of variations in the blood velocity, organization of blood flow and quantification of blood stasis.

Results demonstrated the capabilities of the CFD model to reproduce the expected physiological behavior of the blood flow dynamics inside the LA and the LAA. Velocities within the LA and LAA showed higher values in the NL subjects with respect to PAR-AF and PER-AF patients. The lowest values within the LA and LAA were observed in the PER-AF group that could imply a higher probability of blood stasis and consequently an increase of stroke risk. In PAR-AF patients the contractility was not strongly reduced as for the PER-AF patients thus leading to higher values of the velocities and a stronger LA contraction/expansion. This may reduce the probability of clot formation. Vortex structures, LAA ostium velocity, and the LAA fluid particle analysis confirmed what we qualitatively expected about the differences of the three groups.

These preliminary results on a small cohort of nineteen patients suggest the feasibility of such approach for allowing stroke risk stratification in AF on a patient specific basis.

Acknowledgments

The work was supported by PRIN project Modeling the heart across the scales: from cardiac cells to the whole organ, Prot. 2017AXL54F, funded by the Italian Ministry of Education, University and Research (MIUR).

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