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Left Atrial 4D Flow MRI: Stasis and Velocity Mapping in Patients with Atrial Fibrillation

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Abstract

Objectives—Left atrial (LA) 4D flow MRI was employed to derive anatomic maps of LA stasis, peak velocity, and time-to-peak velocity (TTP) in patients with atrial fibrillation (AF) and to identify relationships between LA flow with LA volume and patient characteristics.

Materials and Methods—4D flow MRI for the in-vivo assessment of time-resolved 3D LA blood flow velocities was performed in 111 subjects: 42 patients with a history of AF and in sinus rhythm (AF-sinus), 39 patients with persistent AF (AF-afib), 10 young healthy volunteers (HV), and 20 age appropriate controls (CTRL). Data analysis included the 3D segmentation of the LA and the calculation of LA stasis, peak velocity and TTP maps. Regional LA flow dynamics were quantified by calculating mean stasis, peak velocity and TTP in the LA center region and the region adjacent to the LA wall.

Results—A sensitivity analysis identified thresholds for global LA stasis ($<0.1\text{m/s}$) and peak velocity (top 5% LA velocities) which detected significant differences between AF patients and controls for global LA stasis (HV=25±5%, CTRL=29±10%, AF-sinus=41±13%, AF-afib=52±17%) and peak velocity (HV=0.43±0.02m/s, CTRL=0.37±0.04m/s, AF-sinus=0.33±0.05m/s, AF-afib=0.30±0.05m/s). Regional analysis revealed significantly increased stasis at both LA center and wall for AF patients compared to age appropriate controls (29%-84% difference, $p<0.006$) and for AF-afib vs. AF-sinus patients (22%-30% difference, $p<0.004$). In addition, stasis close to the LA wall was significantly elevated ($p<0.001$) compared to the LA center for all subject groups. Multiple regressions revealed significant ($R^2_{\text{Adj}}=0.45\text{-}0.50$, $p<0.001$)

relationships between impaired global LA flow (reduced velocity and increased stasis) with age ($|\beta|=0.27-0.50$, $p<0.002$) and LA volume ($|\beta|=0.26-0.50$, $p<0.003$).

Conclusions—Atrial 4D flow MRI detected changes in global and regional LA flow dynamics associated with AF, age and LA volume. Longitudinal studies are needed to test the diagnostic value of LA flow metrics as potential risk factors for thromboembolic events.

Keywords

Atrial fibrillation; 4D flow MRI; left atrium; stasis; peak velocity; stroke

INTRODUCTION

Atrial fibrillation (AF) is the most common cardiac arrhythmia, affecting approximately 33.5 million patients worldwide.¹ The most serious complication from AF is stroke, which is attributed to embolism of thrombus from the left atrium (LA).² Studies utilizing transesophageal echocardiography (TEE) have shown that impaired flow in the LA is an independent risk factor for thrombus formation and stroke in AF.³⁻⁵ Furthermore, presence of spontaneous echo contrast, a marker of blood stasis, has been shown to predict thromboembolism.^{3,6,7} Other TEE studies have shown that LA size and shape may be additional parameters influencing thromboembolic risk.^{8,9,10} However, TEE requires esophageal intubation and the standard 2D imaging cannot fully assess the complex 3D pattern of flow and stasis in the LA.

4D flow MRI can overcome these limitations by providing the ability to noninvasively measure complex 3D blood flow patterns in-vivo¹¹⁻¹³. A number of studies have demonstrated that 4D flow MRI is well suited for the comprehensive assessment of cardiac¹⁴⁻¹⁷ and LA flow dynamics.¹⁸⁻²⁰ Moreover, it has recently been shown that 4D flow MRI can assess LA flow patterns in patients with AF²¹. However, previous studies did not provide an intuitive visualization and quantitative evaluation of LA flow and LA stasis. In addition, information on the choice of thresholds to detect differences in LA flow parameters and LA stasis between groups of AF patients and controls is lacking.

It was the aim of this study to test the potential of novel tools (anatomic maps of LA stasis, peak velocity, and time-to-peak velocity) for the characterization of LA volume and flow, all derived from a single 4D flow MRI scan. We hypothesized that 4D flow derived metrics of LA flow dynamics can detect differences between groups of AF patients and controls and identify relationships between global and regional LA flow, LA volume, and patient characteristics.

METHODS

Study Cohort

A total of 111 subjects were included in the study (81 patients with AF and 30 healthy controls). AF patients included 42 subjects with a history of AF and in sinus rhythm during MR imaging (AF-sinus, age=62±11 years, 13 females) and 39 AF patients who were in AF at the time of imaging (AF-afib, age=66±11 years, 11 females). In addition, 10 young

healthy volunteers (age=24±2 years, 4 females) and 20 age appropriate controls (age=59±7 years, 7 females) were included. All subjects for this HIPAA compliant study were included in the study according to procedures approved by the Northwestern University Institutional Review Board.

MR Imaging

All MRI examinations were performed on 1.5T and 3T MRI systems (Espree, Aera, Avanto, and Skyra, Siemens, Germany). All patients underwent standard-of-care cardiac MRI including retrospectively ECG gated time-resolved (CINE) balanced steady-state free precession (SSFP) imaging in four-chamber, two-chamber, and short axis orientation of the left ventricle to evaluate left ventricular ejection fraction (LVEF). In addition, prospectively ECG gated time-resolved 3D phase-contrast (PC) MRI with three-directional velocity encoding (4D flow MRI) was employed to measure in-vivo 3D blood flow velocities in the LA. 4D flow MRI data were acquired during free breathing using navigator gating of the diaphragm motion.^{18, 22} Further 4D flow MRI pulse sequence parameters were as follows: flip angle=7°, spatial resolution=2.5-3.0mm × 2.5-3.0mm × 3.0-4.0mm, temporal resolution=37.6-41.6ms, imaging acceleration (GRAPPA technique) with a reduction factor of R=2, total acquisition time=10-20min depending on heart rate and navigator efficiency, velocity sensitivity=100-150cm/s. If Gd-contrast administration and contrast enhanced MRA was part of the standard-of-care imaging protocol, 4D flow data was performed at the end of the MRI exam (i.e. 10-15 minutes post Gd-injection). In case of contrast agent administration, the flip angle was adjusted to 15° account for different blood T1.

4D flow MRI Data Analysis

Data pre-processing included corrections for Maxwell terms, eddy current induced phase offsets and velocity aliasing²²⁻²⁴. In addition, 3D PC-MR angiography data were derived from the 4D flow data and used for creating a 3D segmentation of the LA (MIMIC's Materialise, USA)²⁵⁻²⁷. As illustrated in figure 1A, the resulting 3D segmentation mask was used to quantify LA volume and to isolate the velocity data in the LA volume for all atrial voxels and all cardiac time frames. The resulting 4D flow MRI data provides information on 3-directional flow velocities ($v_x(t)$, $v_y(t)$, $v_z(t)$) over the cardiac cycle within the segmented LA volume (t =time in the cardiac cycle). For further hemodynamic analysis, absolute atrial velocities

$$v(t) = \sqrt{v_x(t)^2 + v_y(t)^2 + v_z(t)^2}$$

were calculated for each voxel inside the segmented LA and used to derive LA stasis, peak velocity and time-to-peak (TTP) maps oriented in sagittal oblique orientation as illustrated in figure 1B. Mean LA velocity (averaged over all LA voxels and cardiac time frames) was calculated.

Atrial stasis maps—For each voxel inside the segmented LA, the relative amount of flow stasis r_{stasis} (in %) was calculated by determining the number of cardiac time frames n_{stasis} with velocities below a threshold ($v(t) < v_{\text{stasis_thresh}}$) normalized by the total number of

cardiac time frames N_{Tot} : $r_{stasis} = n_{stasis} / N_{Tot} * 100$. Stasis maps were generated by projecting the mean relative stasis on a 2D plane transecting the LA and were color-coded for intuitive identification of regions with low vs. high stasis (figure 1B, left).

Peak LA velocity 4D MIPs—For each voxel inside the segmented LA, the maximum velocity (v_{max}) within the cardiac cycle was extracted. The maximum intensity projection (MIP) over all v_{max} was calculated resulting in a 4D (3D+time) MIP of LA peak velocities (figure 1B, mid).

TTP maps—To quantify regional differences in timing of high LA flow velocities with respect to the beginning of the cardiac cycle (as defined by the R-wave), the time-to-peak (TTP) velocity for each voxel inside the segmented LA was determined. TTP maps were generated by projecting mean TTP on a 2D plane (figure 1B, right).

All maps were overlaid onto the underlying anatomic 4D flow MRI data for improved anatomic orientation (see figure 1B). To evaluate inter-observer variability, a second independent observer, blinded to the other reader's results, re-analyzed the LA 4D flow data by performing a second 3D segmentation of the LA in a subgroup of 29 subjects.

Quantification of Global and Regional Metrics of LA Flow Dynamics—Global stasis and TTP for the entire LA were calculated by averaging over all LA voxels. The overall peak LA velocity was calculated as the average over the top $v_{peakvel_thresh}\%$ of all LA velocities (3D and time over the cardiac cycle). As the pathophysiology of thromboembolism in AF is based upon formation of mural thrombi, regional analysis focused on the region adjacent to the left atrial wall. As illustrated in figure 1B, regional LA flow analysis was performed on all three LA maps (stasis, peak velocity, TTP) by dividing the LA in two regions: the LA center region and the region adjacent to the LA wall. In all subjects, the LA center region was automatically generated without user interaction by eroding the segmented LA area by 2 voxels inward from the outer LA boundaries. Subsequently, the region adjacent to the LA wall was calculated by subtracting the LA center region from the original LA segmentation. Average peak velocity, stasis, and TTP were calculated in both regions for all subjects.

Statistics - Sensitivity Analysis: Identification of LA Stasis and LA Peak Velocity Thresholds

All data were analyzed using a range of different velocity thresholds ($v_{stasis_thresh} = [0.02\text{m/s} - 0.2\text{m/s}]$ in 0.02 m/s steps and $v_{peakvel_thresh} = [1\% - 10\%]$ in 1% steps) to assess their influence on LA flow parameters and differences in LA flow dynamics between groups (young and older controls, AF-sinus, AF-afib). For each group, a Shapiro-Wilk test was used to determine if parameters were normally distributed. To compare parameters among the four groups, 1-way ANOVA (Gaussian distribution) or Kruskal Wallis (non-Gaussian distribution) was employed. If these tests determined that a parameter was significantly different among groups ($p < 0.05$), multiple comparisons between groups were performed using independent-sample t-tests (Gaussian distribution) or Mann-Whitney tests (non-

Gaussian distribution). Bonferroni correction was used to adjust for multiple comparisons and differences were considered significant for $p < 0.0125$.

Statistics - Relationships between LA Flow Metrics and Patient Characteristics

To identify relationships between metrics of LA flow (mean velocity, peak velocity, stasis, TTP) with demographic and geometric parameters (age, heart rate, LVEF, LA volume), Pearson's correlation coefficients r were calculated to identify variables for subsequent multiple linear regression analysis ($r \geq 0.25$). The aim was to quantify the relationship between impaired LA flow metrics (dependent parameters) and demographics and geometric parameters as independent predictors. The overall quality of the model was quantified using the adjusted R-squared (R^2_{adj}). The relative contributions of the demographic and geometric parameters were determined from the standardized regression coefficients β . A correlation was considered significant for $p < 0.05$.

RESULTS

Patient Characteristics

Patient demographics are summarized in table 1. The AF population was predominantly male and AF cohorts had significantly increased LA volumes compared to the age appropriate controls. In addition, LA volume (64 ± 29 ml vs. 93 ± 58 ml, $p = 0.005$) and heart rate (68 ± 15 bpm vs. 78 ± 15 bpm, $p = 0.003$) were significantly higher in AF-afib patients compared to AF-sinus subjects.

Left Atrial Stasis, Peak Velocity and Time-to-Peak Maps

Examples of LA flow parameter maps (stasis, peak velocity, TTP) for four representative subjects of each cohort are shown in Figure 2. 4D flow MRI in a young healthy volunteer (figure 2A) revealed high peak velocities throughout the LA and lowest stasis compared to the three subjects from other groups. In all subjects, LA stasis based on a velocity threshold of 0.1 m/s showed an inhomogeneous pattern and was higher adjacent to the LA wall compared to the central region of the LA which was confirmed by regional LA stasis quantification (see mean stasis for LA center and LA wall below individual maps). The age appropriate control subject (figure 2B) showed similar regional LA stasis patterns but considerably reduced LA peak velocities in both LA regions (average reduction by 38% and 34%, respectively). AF patients (figures 2C and D) showed higher stasis throughout the LA (particularly adjacent to the LA wall) and lower and more heterogeneous distribution of LA peak velocities (specifically for AF-afib, figure 2D) compared to control subjects. TTP did not show consistent differences among groups.

Sensitivity Analysis: Identification of LA Stasis and LA Peak Velocity Thresholds

Figure 3 shows the results of the analysis of different thresholds for global LA stasis and peak velocity quantification. Except for young vs. age appropriate controls, LA stasis (figure 3A) was significantly different between each of the groups (age matched controls, AF-sinus, AF-afib) for $v_{stasis_thresh} \geq 0.04$ m/s. LA stasis could robustly differentiate between these groups for a wide range of velocity thresholds ($p \leq 0.001$ for v_{stasis_thresh} ranging from 0.10-0.18 m/s). Findings for LA peak velocities are shown in figure 3B. Significant

differences ($p < 0.0125$) between each of the groups were found for a wide range of thresholds $v_{\text{peakvel_thresh}} = 3\%$ (except for AF-sinus vs. age appropriate controls). For further analysis of global LA stasis and peak velocity, $v_{\text{stasis_thresh}} = 0.1 \text{ m/s}$ and $v_{\text{peakvel_thresh}} = 5\%$ were chosen, respectively.

Group wise Comparisons of Global Metrics of LA Flow

For all analyzed global LA flow metrics (LA mean velocity, stasis, peak velocity, TTP) significant differences across all four groups were found (ANOVA or Kruskal Wallis, $p < 0.0001$). Subsequent multiple comparisons between groups (table 2) demonstrated significant differences ($p < 0.0125$) for LA mean velocity, stasis, and peak velocity except for peak LA velocities between age matched controls vs. AF-sinus patients ($p = 0.026$).

Regional LA Velocities and Stasis

The results of the regional analysis of LA flow dynamics (LA center versus regions adjacent to the LA wall) are summarized in table 3 and figure 4. Multiple comparisons (table 3) demonstrated significantly increased stasis in all regions for both AF patient groups (AF-sinus, AF-afib) compared to age appropriate controls (29%-84% difference, $p < 0.006$) and for AF-afib compared to AF-sinus patients (22%-30% difference, $p < 0.004$). As illustrated in figure 4, flow stasis adjacent to the LA wall was significantly elevated ($P < 0.001$) compared to the LA center for all four subject groups. Regional peak velocities were generally lower for AF patients compared to controls and reduced adjacent to the LA wall compared to the LA center which was, however, only significant for age appropriate controls and AF-afib patients (figure 4).

Relationships between LA Flow Metrics and Patient Characteristics

As summarized in Table 4, multiple linear regressions revealed significant relationships ($p = 0.002$) between reduced global mean and peak LA velocities and age and LA volume but not with heart rate. Similarly, the extent of the LA exposed to flow stasis demonstrated significant relationships with age and LA volume but not with heart rate.

Inter-Observer Variability

Bland-Altman plots demonstrated good inter-observer agreement for measurements of mean LA velocity, peak LA velocity, and LA stasis (Figure 5). Observer variability resulted in average inter-observer differences of 6.0% for mean velocity, 10.2% for global LA stasis, and 7.9% for global LA peak velocity.

DISCUSSION

The findings of this study demonstrate the potential of 4D flow MRI for the comprehensive assessment of global and regional LA flow dynamics. The analysis to identify velocity thresholds for LA stasis and LA peak velocity that could differentiate among all four patient and controls groups revealed a wide range of significant thresholds, supporting the robustness of the technique. In addition, regional stasis was consistently elevated adjacent to the LA wall compared to the LA center in all study groups and was significantly elevated for AF patients compared to controls. These results indicate the potential of atrial 4D flow MRI

to detect differences in global LA stasis and LA peak velocity related to rhythm (sinus versus AF) in patients with AF and regional differences in stasis related to LA flow physiology (reduced flow and elevated stasis adjacent to the LA wall). Moreover, significant associations of impaired LA flow (reduced mean and peak velocity and increased stasis) with LA volume point to a physiologic structure-function relationship between altered LA geometry and hemodynamics.

It was initially hypothesized that LA time-to-peak (TTP) velocity might be a useful measure to detect disorganized flow in patients with AF (inconsistent timing of the occurrence of peak velocity across the LA). However, neither global nor regional LA TTP velocity was sensitive to detect differences in LA flow patterns. Based on these findings we speculate that reduction of LA peak velocities and in particular increase in regional LA stasis are more sensitive markers of altered LA flow compared to the simple measure of the timing of LA flow (TTP) used in this study.

4D flow MRI has previously been applied for the in-vivo study of left atrial blood flow in a number of studies^{12, 13, 18-20, 28, 29}. The technique is noninvasive and provides time-resolved 3D LA blood flow velocities with full volumetric coverage of the LA. Previous studies were either based on small cohorts to evaluate normal and pathological flow physiology, such as the presence and extent of vortex flow, in the heart and atria^{12, 19, 20}, to study the asymmetric redirection of flow through the entire heart¹³, or to assess the impact of atrial-septal defects and shunt flows²⁹. A recent study by Suwa et al. investigated the relationship between left atrial vortex flow, heart diseases and LA volume²⁸. Similar to findings in our study, the authors found associations between changes in LA flow and volume.

Previous studies, however, were based on 3D blood flow visualization (using vector fields, time resolved pathlines, or streamlines) and qualitative evaluation of flow features (semi-quantitative schemes to grade atrial vortex flow) or regional flow quantification based on 2D analysis planes. In contrast, our study utilized the complete three-directional velocity information in the entire LA and over the cardiac cycle to visualize LA flow using maps that quantify metrics reflecting 4D (3D + time) flow parameters. 4D flow derived stasis maps and peak velocity 4D MIPs are a new concept offering intuitive visualization of otherwise complex 4D flow MRI data. In addition, 3D segmentation of the LA enabled an automated regional analysis of LA flow dynamics by systematic inward erosion of the map area and calculation of velocities and stasis in the LA center and a 2-voxel region adjacent to the LA wall. Such patient specific maps in conjunction with regional quantification could potentially identify regions with elevated stasis which are thought to promote thrombus formation and thus risk for stroke. Such regional information could be useful when considering therapies for stroke prevention in AF that address only localized areas, such as left atrial appendage (LAA) occlusion devices. Future studies should include a more detailed assessment of regional differences in LA flow patterns (e.g. LA vs LAA velocities and stasis) to further elucidate the role of regional variability of LA flow and stasis in left atrial thrombus formation. These studies can also help to better define the diagnostic value of reducing the LA flow information into a single parameter (e.g. global LA stasis or global LA peak velocity) versus maintaining a 2D stasis map for additional visual interpretation.

A number of Doppler echocardiography studies have previously investigated LA blood flow velocities. In a TEE study with 721 AF patients, Goldman et al³ reported reduced peak LA appendage velocity in patients with AF compared to those in sinus rhythm during TEE (33cm/s vs. 61cm/s, $p<0.001$). The selection of velocity thresholds for the sensitivity analysis in our study was based on results from this TEE study which found that peak antegrade left atrial appendage (emptying) flow velocity $<0.2\text{m/s}$ was associated with increased risk for atrial thrombus formation and embolic stroke³. Another study by Handke et al⁴ also found significant differences in LA peak velocities among patients with sinus rhythm ($71\pm16\text{ cm/s}$), and with cardiac arrhythmia during TEE ($46\pm13\text{cm/s}$). In agreement with these studies, our patient cohort exhibited differences in LA flow velocities between AF patients in sinus rhythm and with cardiac arrhythmia during 4D flow MRI. However, LA peak velocities in our study cohort were lower ($0.30\text{-}0.43\text{m/s}$) compared to findings in previous TEE studies. This underestimation of peak velocities may be attributed to the lower spatial and temporal resolution of 4D flow MRI compared to TEE. Nevertheless, both 4D flow derived LA peak velocity and LA stasis could detect significant differences between AF patient and control groups

Study Limitations

The present study evaluated LA velocity maps measured with 4D flow MRI in patients with atrial fibrillation (paroxysmal vs. persistent), healthy volunteers and age-matched controls. The main limitation of this study is related to its cross-sectional design. Clinical risk scores or data on other factors that may affect LA velocity maps such as mitral regurgitation or stenosis were not available. In addition, information on mitral valve function and diastolic dysfunction was not available for the AF patients in our study cohort. Furthermore, no follow-up in terms of intra-LA thrombus formation was performed which was beyond the scope of this feasibility study. Additional longitudinal studies are thus needed to further test the diagnostic value of 4D flow derived LA for metrics for risk stratification of AF patients for future thromboembolic events.

Our study demonstrated significant associations between LA volume and LA velocities and stasis. However, a more detailed analysis of LA and LAA geometry and shape and its association with LA flow parameters was not performed. Our study design was based on an analysis workflow targeting a cardiac region (the left atrium) that could reliably be segmented and analyzed based on the 4D flow MRI imaging contrast and spatial resolution - as was demonstrated by the very good observer variability we found in our study. In this context, additional studies need to be conducted to investigate if the contrast and resolution of 4D flow data will be sufficient to identify the LAA boundaries for a reliable assessment of LAA size, anatomy, and flow dynamics. Future studies should thus systematically evaluate differences in LA vs. LAA flow dynamics and test the feasibility, reproducibility and observer variability of the quantification LAA size, anatomy and flow dynamics based on 4D flow MRI.

A further limitation is related to the selection of the velocity sensitivity (venc) of the 4D flow MRI acquisition which was in the range of $100\text{-}150\text{cm/s}$ (i.e. larger than typical atrial flow velocities) to avoid velocity aliasing. However, no velocity scout scan was performed

to better tailor the venc to the atrial velocities in the individual patient to optimize the velocity-to-noise ratio of the LA 4D flow data. Another drawback is the long scan times on the order of 10-20 minutes needed to collect atrial 4D flow MRI data. As a result, beat-to-beat flow variations in AF patients with cardiac arrhythmia cannot be captured by this technique. Nevertheless, the blood flow measurements made with 4D flow MRI represent the average flow patterns over the entire length of the acquisition that are consistent over several cardiac cycles. This underlying assumption was confirmed by a recently performed validation study ²¹. Based on real time in-vivo TEE data in 5 AF patients with known arrhythmia, a simulation study systematically investigated the impact of beat-to-beat variations on ECG gated multi-beat flow imaging with MRI. Results demonstrated that ECG gated multi-beat flow MRI in patients with cardiac arrhythmia could reproduce persistent average LA and left ventricular mean velocities within 7.0-7.4% compared to TEE. These findings demonstrate that 4D flow MRI can reliably assess persistent atrial flow and stasis patterns that are consistently present over multiple heart beats. Since LA thrombus, the main source of embolic stroke in AF patients, will form over longer periods of time, we speculate that these persistent flow features representing long-term patterns over multiple RR intervals (e.g. elevated LA stasis) could be important physiologic markers for thrombus formation and this thromboembolic risk.

Conclusion

The findings of this study indicate that atrial 4D flow MRI and derived in-vivo peak velocity and stasis maps are robust tools for the detection changes in global and regional flow dynamics in the left atrium associated with atrial fibrillation, patient age and left atrial volume. Additional longitudinal studies are warranted to test the diagnostic value of LA flow metrics as potential risk factors for thromboembolic events.

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Figure 1.

4D flow MRI data analysis in a 62 year old male patient with a history of AF (AF-sinus, subject #35) including A: 3D segmentation of the left atrium (LA) based on the 3D-PCMRA data (gray shaded iso-surface) and masking of velocities inside the segmented LA. B: Calculation of LA stasis maps for a velocity threshold of 0.1m/s (left), peak velocity maximum intensity projections (MIPs, mid), and time-to-peak velocity (TTP) maps. Atrial areas for the analysis regional velocities and stasis in the LA center and adjacent to the LA wall are delineated by black lines. The mean for all three metrics of regional LA flow dynamics are listed below each map. AAo = ascending aorta, DAAo = descending aorta, PA = pulmonary artery.

Figure 2.

Maps of left atrial flow parameters superimposed on the underlying anatomic 4D flow MRI data in oblique sagittal orientation. The individual images show stasis maps for a velocity threshold of 0.1 m/s (left column), peak velocity maximum intensity projections (4D MIPs, mid column), and time-to-peak (TTP) velocity maps (right column) in four subjects representing each of the sub-groups (A-D). Color coding illustrates regions in the LA with high (red) and low (blue) stasis, peak velocity and TTP. Areas for the analysis of regional flow dynamics (LA center and LA wall) are delineated and the resulting regional LA stasis, peak velocities and TTP are listed below each map. AAo = ascending aorta, PA = pulmonary artery, LA = left atrium.

Figure 3. Sensitivity analysis for the identification of LA stasis and LA peak velocity thresholds. **A:** LA stasis (top) as a function of the LA velocity threshold (% LA velocities < LA velocity threshold, $v_{\text{stasis_thresh}}$) for all four groups (young volunteers, age appropriate controls, AF-sinus, AF-afib). Corresponding p-values for pair-wise comparisons of LA stasis between groups are shown below. **B:** Peak LA velocities (top) for different thresholds (% of top LA velocities, $v_{\text{peakvel_thresh}}$) and p-values for between group comparisons (bottom). The individual data points represent averaged over all subjects in each group. Error bars indicate inter-individual standard deviations of LA flow metrics. LA = left atrium.

Figure 4.

Group wise comparisons of regional LA peak velocities (A) and LA stasis (B). Flow stasis adjacent to the LA wall was significantly elevated compared to the LA center for all subject groups. The individual box plots illustrate the median (central mark) and the 25th and 75th percentiles (edges), the whiskers extend to the most extreme data points not considered outliers, and outliers are plotted individually as '+'.

Figure 5.

Bland Altman analysis of inter-observer variability for the quantification of mean LA velocity, peak LA velocity ($v_{\text{peakvel_thresh}}=5\%$) and LA stasis ($v_{\text{stasis_thresh}}=0.1\text{m/s}$) in a subgroup of $n=29$ subjects.

Table 1

Demographics of study cohorts. Differences between groups were considered significant for $p < 0.0125$ (Bonferroni correction for multiple comparisons).

	N	age [years]	gender [male/female]	LVEF [%]	LA volume [ml]	heart rate [bpm]
young controls	10	24 ± 2	6 / 4	62 ± 4	25 ± 5	63 ± 8
age controls	20	59 ± 7	13 / 7	62 ± 1	37 ± 12 [*]	68 ± 11
AF-sinus patients	42	62 ± 11	29 / 13	58 ± 8	64 ± 29 [#]	68 ± 15
AF-afib patients	39	66 ± 11	27 / 11	54 ± 10 ⁺	93 ± 58 ^{+\$}	78 ± 15 ^{\$}

* significant difference old vs. young controls

significant difference old controls vs. AF-sinus

+ significant difference old controls vs. AF-afib

\$ significant difference AF-sinus vs. AF-afib

Table 2

Descriptive statistics for **global** metrics of left atrial (LA) flow dynamics. Differences between groups were considered significant for $p < 0.0125$ (Bonferroni correction for multiple comparisons).

	N	mean LA vel [m/s]	stasis <0.1 m/s [%]	peak vel 5% [m/s]	TTP [ms]
young controls	10	0.18±0.02	25±5	0.43±0.02	480±50
age controls	20	0.16±0.02 [*]	29±10	0.37±0.04 [*]	410±60 [*]
AF-sinus patients	42	0.13±0.02 [#]	41±13 [#]	0.33±0.05	420±90
AF-afib patients	39	0.11±0.03 ^{+\$}	52±17 ^{+\$}	0.30±0.05 ^{+\$}	400±90

^{*} significant difference age appropriate vs. young controls

[#] significant difference age appropriate controls vs. AF-sinus

⁺ significant difference age appropriate controls vs. AF-afib

^{\$} significant difference AF-sinus vs. AF-afib

Table 3

Summary of the results of regional LA flow analysis based on stasis, peak velocity and TPP maps. Differences between groups were considered significant for $p < 0.0125$ (Bonferroni correction for multiple comparisons).

	N	regional stasis <0.1 m/s [%]		regional mean peak velocity [m/s]		regional mean TTP [ms]	
		center	wall	center	wall	center	wall
young controls	10	23±5	32±4	0.59±0.09	0.54±0.09	482±53	463±52
age controls	20	28±10	36±8	0.44±0.10 [*]	0.40±0.11 [*]	411±63 [*]	396±59 [*]
AF-sinus patients	42	39±13 [#]	46±14 [#]	0.41±0.09	0.39±0.11	425±86	386±88
AF-afib patients	39	51±17 ^{+\$}	56±16 ^{+\$}	0.36±0.09 ⁺	0.31±0.10 ^{+\$}	408±93	381±88

^{*} significant difference age appropriate vs. young controls

[#] significant difference age appropriate controls vs. AF-sinus

⁺ significant difference age appropriate controls vs. AF-afib

^{\$} significant difference AF-sinus vs. AF-afib

Table 4

Multiple linear regressions of global LA flow metrics with heart rate, age, and LA volume as independent predictors in n=111 subjects. The significance of the model was assessed using the overall p-value, and the percent of variance explained using the adjusted R^2 (R^2_{Adj}). The relative contributions of the geometric parameters are given by the standardized regression coefficients β . Significant correlations ($p < 0.05$) are indicated by bold numbers (NS = not significant).

LA flow metric	model quality		age		heart rate		LA volume	
	R^2_{Adj}	p-value	β	p-value	β	p-value	β	p-value
mean LA vel	0.50	<0.001	-0.42	<0.001	-0.09	NS	-0.39	<0.001
stasis < 0.1 m/s	0.45	<0.001	0.27	0.001	0.09	NS	0.50	<0.001
peak vel, 5%	0.46	<0.001	-0.50	<0.001	-0.10	NS	-0.26	0.002