Europace (2014) **16**, 1546–1553
doi:10.1093/europace/euu047

Clinical correlates of echocardiographic tissue velocity imaging abnormalities of the left atrial wall during atrial fibrillation

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Received 23 October 2013; accepted after revision 7 February 2014; online publish-ahead-of-print 25 March 2014

Aims In patients with atrial fibrillation (AF), echocardiographic tissue velocity imaging (TVI) enables assessment of electrical and structural remodelling by measuring, respectively, the AF cycle length (AFCL-TVI) and the atrial fibrillatory wall motion velocity (AFV-TVI). We investigated the clinical and echocardiographic correlates of atrial remodelling assessed by TVI.

Methods and results We studied 215 patients presenting with AF. In all patients, we measured the AFCL-TVI and the AFV-TVI in the left atrium. Standard baseline characteristics were recorded. We divided patients by median value of AFV-TVI and AFCL-TVI to evaluate the determinants of atrial remodelling. A low AFV-TVI was related with a longer median duration of the current AF episode, a higher prevalence of significant mitral regurgitation and a thicker left ventricle (LV). Multivariate analysis revealed that a low AFV-TVI was independently associated with a longer median duration of the current AF episode [OR 0.09 (95% CI 0.03–0.027); $P < 0.001$]. Univariately, a short AFCL-TVI was associated with a long median duration of the current AF episode, the use of anti-arrhythmic drugs, a lower LV ejection fraction (LVEF) and a smaller left atrial volume index (LAVI). Multivariate analysis revealed that LVEF [OR 1.48 (95% CI 1.09–2.01); $P = 0.013$] and LAVI [OR 1.37 (95% CI 1.08–1.74); $P = 0.010$] were independently associated with AFCL-TVI.

Conclusion This study investigated the clinical and echocardiographic correlates of atrial remodelling assessed by TVI. The AFV-TVI is reduced in patients with a long AF duration and who have mitral regurgitation. In addition, the AFCL is long if LAVI is high and LVEF preserved. Tissue velocity imaging parameters measured during AF may be helpful to characterize the degree of atrial remodelling and optimize treatment.

Keywords Atrial fibrillation • Atrial substrate • Echocardiography

Introduction

Atrial fibrillation (AF) is associated with electrical and structural remodelling.[1] Atrial remodelling mostly starts in the left atrium (LA)[2] and may set the stage for enhanced thrombogenesis and stroke, and increased mortality.[3–5] Determining the degree of atrial remodelling is important since it is associated with arrhythmia prognosis and response to therapy.[6–8] Although echocardiographic atrial size is an important marker for AF onset,[9] AF progression[10] as well as stroke risk in AF,[11] more independent predictors with a high predictive value are needed. Previously, we showed that echocardiographic tissue velocity imaging (TVI) may be used to assess electrical remodelling through measuring the atrial fibrillatory cycle length (AFCL-TVI), which represents the atrial refractoriness.[6,12] Atrial fibrillation cycle length determined by tissue velocity imaging correlated well with the AFCL as measured during an invasive electrophysiological study.[6] Apart from electrical remodelling, AF is also associated with structural remodelling which is characterized by diminished atrial fibrillatory contractility of the atrial wall.[3,4] The intrinsic contractility of the fibrillating atrial wall may be measured using echocardiographic TVI of atrial fibrillatory wall velocity (AFV-TVI). We reasoned that direct non-invasive echocardiographic visualization

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What's new?

- Tissue velocity imaging (TVI) parameters may be helpful to characterize the degree of atrial remodelling.
- A low atrial fibrillatory wall motion velocity determined by TVI (AFV-TVI) is associated with longer AF duration and the presence of mitral regurgitation independent from other clinical parameters.
- A long atrial fibrillation cycle length determined by TVI (AFCL-TVI) is related to a higher left atrial volume index and a normal left ventricular ejection fraction.
- Measuring AFV-TVI and AFCL-TVI can help to predict response to therapy.

by TVI of the atrial wall during AF might further enhance our knowledge on the clinical significance of atrial remodelling in AF. Better insights in the atrial remodelling may help clinicians to choose the right therapy (antithrombotic treatment, rhythm control, and rate control) for the right patient. In this study, we investigated the clinical and echocardiographic correlates of atrial remodelling assessed with echocardiographic TVI during AF.

Methods

Study population

In this retrospective, cross-sectional study, we included 309 patients presenting with acute AF at the first heart aid or admitted with persistent AF for elective electrical cardioversion between 2006 and 2012 in the Maastricht University Medical Centre and in whom trans-thoracic echocardiography was performed during AF. We excluded 94 (31%) patients because atrial TVI parameters could not be assessed due to a too high ventricular rate. The 215 remaining patients were included for further analysis in this study. Patient characteristics, including demographics, history, and medication were collected from patient charts and electronic medical records. This study was approved by the Institutional Review Board and complied with the declaration of Helsinki. Patient written informed consent was obtained.

Echocardiographic examination

Trans-thoracic echocardiography was performed during AF in all patients prior to start of treatment (maximum of 4 h). We obtained the colour TVI images of the LA in an apical four chamber view with the patient in supine position using a Vivid7 ultrasound system (GE Healthcare, Milwaukee, WI, USA) with a 3.5 MHz cardiac transducer as described previously.[6] The frame rate was set above 100 Hz. Using commercially available software (Q-analysis, GE Healthcare), during the late diastole (between the end of E′ wave and start of S'' wave) we analysed colour TVI curves obtained offline from the lateral wall of the LA just above the mitral annulus. At that point, we measured the atrial fibrillatory cycle length (AFCL-TVI) and atrial fibrillatory wall velocity (AFV-TVI) using the colour TVI curves (*Figure 1*). The researcher was blinded to the patient characteristics. Atrial fibrillation cycle length determined by tissue velocity imaging was defined as the time interval between two consecutive negative deflections of the late diastolic atrial tissue velocity curve and the average of at least three AFCL-TVI's was reported. The AFV-TVI was defined as the highest difference in velocity of negative and positive deflections of the late diastolic atrial tissue velocity curve.

As mentioned before, in 94 patients measurement of the TVI parameters was not possible due to a too high ventricular rate which precludes TVI analysis of the atrial wall due to interference with ventricular motion. These patients were excluded for further analysis. Additionally, all patients underwent standard echocardiography according to the recommendations as described in the European Echocardiography guidelines.[13] The degree of mitral regurgitation (MR) was assessed by the standard protocol of our hospital based on a combination of proximal isovelocity surface area, vena contracta, systolic backflow in the pulmonary veins, and the effective regurgitant orifice (ERO) area according to the recommendations of the European Association of Echocardiography.[14] We graded the MR as follows: grade 0—no MR; grade 1—mild MR (ERO < 0.2 cm^2); grade 2—mild-to-moderate MR (ERO 0.2–0.3 cm^2); grade 3—moderate-to-severe MR (ERO 0.3–0.4 cm^2); and grade 4—severe MR (ERO > 0.4 cm^2). Significant mitral valve regurgitation was defined as echocardiographic mitral valve regurgitation grade 2 or more.

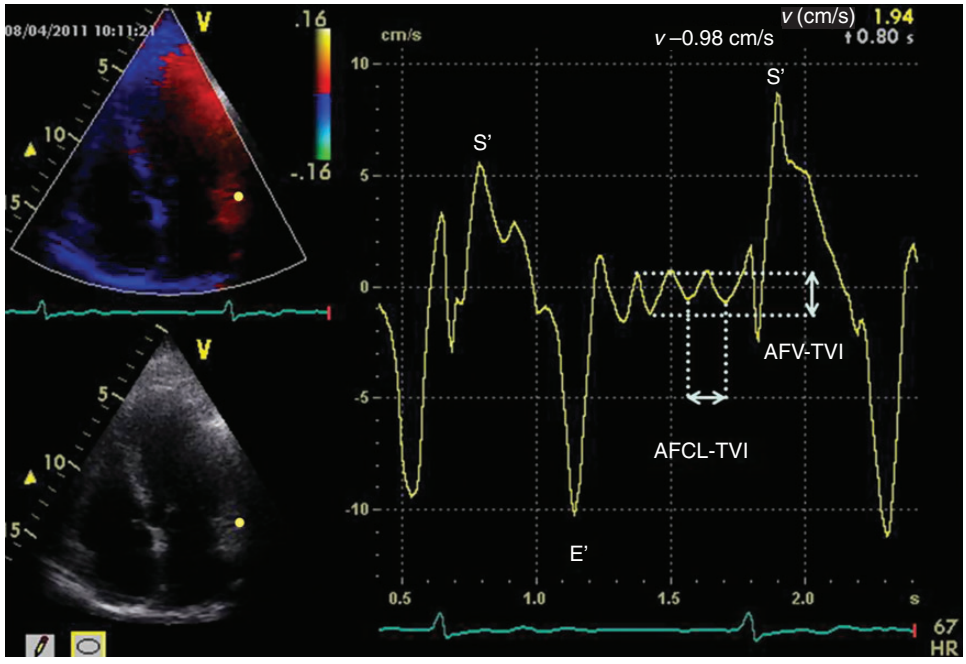
Statistical analysis

To compare patient characteristics in patients with or without significant electrical and structural remodelling, we divided patients by median value of AFV-TVI and AFCL-TVI. Data analysis was performed using SPSS statistical software (SPSS, version 18.0). Continuous variables are reported as 'mean $\pm$ standard deviation' when normally distributed and as 'median (25th percentile–75th percentile)' when no normal distribution was present. Categorical variables are reported as 'observed number of patients (percentage)'. Differences between variables that were not normally distributed were tested with the Mann–Whitney *U* test when comparing two groups and the Kruskal–Wallis test when comparing three groups. Categorical variables were tested with Fisher's exact test when comparing two groups and χ^2 when comparing three groups. To evaluate the relationship between the different parameters, the Spearman's correlation test was used when there was no normal distribution. All parameters with a *P*-value < 0.1 resulting from the univariate comparisons in *Table 1* were included in the linear regression model for multivariate analysis. Linear regression was performed by stepwise exclusion of variables from the model with a *P*-value < 0.05 in the final model. Collinearity and interactions among covariates were checked and none were significant. Medication was not included in the multivariate analysis since it is a reflection of the underlying diseases already included in the model.

Results

Patients characteristics

We analysed 215 patients with a median age of 68 (59–74) years and 156 (73%) being male. In 16 of the 215 patients, measurement of the AFCL-TVI was not possible because of too low amplitude of the TVI signal despite a long diastole. These patients had an AFV-TVI of 0.1 cm/s, the so-called mechanical non-fibrillatory LA. The median AFCL-TVI was 150 [inter-quartile range (IQR) 130–170] ms and the median AFV-TVI was 1.56 (IQR 0.80–2.91) cm/s. Clinical characteristics of the total study population are shown in *Table 1*. The distribution of underlying cardiovascular disease and stroke risk—as indicated by the cumulative $CHADS_2$ score—were representative for a clinical AF population. Most patients in this study had persistent AF (83%), which relates to the fact that all electro-echocardiographic measurements were performed during AF. Only 22% of all patients were treated with an anti-arrhythmic drug (AAD) at the time of echocardiographic measurements.



AFCL-TVI *Atrial fibrillatory cycle length determined by tissue velocity imaging*
AFV-TVI *Atrial fibrillatory wall motion velocity determined by tissue velocity imaging*

Figure 1 Measurement of TVI parameters. AFCL-TVI, atrial fibrillatory cycle length determined by tissue velocity imaging; AFV-TVI, atrial fibrillatory wall motion velocity determined by tissue velocity imaging.

Clinical correlates of atrial fibrillation cycle length determined by tissue velocity imaging

Table 1 shows that patients with a low AFV-TVI had a longer median duration of the current episode of AF and a higher prevalence of significant MR. A low AFV-TVI was also associated with left ventricular hypertrophy (LVH). The distribution of AADs was similar among low and high AFV-TVI groups. Of note, except for mitral valve regurgitation, there was no association between AFV-TVI and underlying cardiovascular diseases. Also, the $CHADS_2$ score was not different among low and high AFV-TVI groups. In the multivariable analysis duration of current AF episode, the presence of significant MR and heart rate remained statistically significant (*Table 2*).

Patients with mechanical non-fibrillatory LA ($n = 16$) were older, i.e. 72 (69–76) vs. 67 (59–74) years ($P = 0.036$), and more often were female (56 vs. 25%, $P = 0.016$) compared with patients with any contractility ($n = 199$). In addition, they were more often diabetic (31 vs. 10%, $P = 0.026$). Patients with mitral valve regurgitation had more often mechanical non-fibrillatory LA compared with patients who had no significant MR [6/39 (15%) vs. 10/173 (6%), $P = 0.08$]. The severity of the MR correlated with AFV-TVI [grade 0 (46%): 1.9 (0.9–3.7) cm/s; grade 1 (36%): 1.5 (0.9–2.8) cm/s; grade 2 (16%): 1.1 (0.5–1.8) cm/s; and grade 3 (2%): 0.6 (0.4–1.9) cm/s; $P = 0.006$]. Left atrial diameter increased with increasing severity of mitral valve regurgitation [grade 0: 43 (39–47); grade 1: 45 (42–49); grade 2: 46 (43–50); grade 3: 52 (50–55); $P = 0.001$). Other echocardiographic parameters did not differ between MR severity categories.

Clinical correlates of Atrial fibrillation cycle length determined by tissue velocity imaging

A short AFCL-TVI was associated with a long median duration of the current episode of AF. Use of AADs was seen more frequently in the subgroup with long AFCL-TVI. This concerned primarily amiodarone and flecainide rather than sotalol (*Table 1*). Left ventricular ejection fraction was slightly but significantly lower in patients with short AFCL-TVI. In addition, low LA volume index was significantly associated with short AFCL-TVI. Multivariable linear regression analysis revealed that left ventricular (LV) ejection fraction (LVEF) and LA volume index were independently associated with AFCL-TVI (*Table 2*).

Further observations

There was a significant relationship between atrial fibrillatory velocity and atrial fibrillatory cycle length as measured with TVI ($P < 0.001$, *Figure 2*). When comparing patients with paroxysmal AF (PAF) with patients with persistent AF, both AFV-TVI and AFCL-TVI were significantly higher and longer in patients with PAF compared with patients with persistent AF (*Figure 3*), respectively. The PAF patients had also significantly more severe MR, a lower LVEF and a greater LA volume (*Figure 3*).

Discussion

This study shows that left atrial contractility, as represented by AFV-TVI, is reduced in patients with a long AF duration and with

Table 1 Characteristics of the study patients

	All (*N* = 215)	AFV-TVI ≤1.56 cm/s (*N* = 108)	AFV-TVI >1.56 cm/s (*N* = 107)	*P*-value	AFCL-TVI <150 ms (*N* = 98)	AFCL-TVI ≥150 ms (*N* = 101)	*P*-value
Age (years)	68 (59–74)	69 (61–74)	66 (58–72)	0.14	67 (58–73)	67 (60–74)	0.28
Current AF episode (days)	91 (32–158)	107 (60–172)	58 (0.4–154)	<0.001	122 (50–182)	70 (2–117)	<0.001
Total AF history (months)	7 (4–34)	6 (3–31)	7 (4–47)	0.07	7 (4–31)	7 (4–44)	0.39
Paroxysmal AF (%)	36 (17%)	3 (3%)	33 (31%)	<0.001	11 (11%)	25 (25%)	0.016
Male	156 (73%)	78 (72%)	78 (73%)	1.00	79 (81%)	70 (69%)	0.07
Medical history							
Hypertension	121 (56%)	61 (57%)	60 (56%)	1.00	54 (55%)	58 (57%)	0.78
Coronary artery disease	66 (31%)	35 (32%)	31 (29%)	0.66	26 (27%)	32 (32%)	0.44
Heart failure	43 (20%)	24 (22%)	19 (18%)	0.50	23 (24%)	18 (18%)	0.38
Ischaemic stroke/TIA	17 (8%)	13 (12%)	5 (5%)	0.13	8 (8%)	8 (8%)	1.00
Diabetes mellitus	25 (12%)	14 (13%)	11 (10%)	0.67	7 (7%)	13 (13%)	0.24
COPD	8 (4%)	4 (4%)	4 (4%)	1.00	5 (5%)	2 (2%)	0.27
Significant mitral valve regurgitation (≥grade 2)	39 (18%)	28 (26%)	11 (10%)	0.004	19 (19%)	14 (14%)	0.34
Mitral stenosis	7 (3%)	5 (5%)	2 (2%)	0.45	2 (2%)	4 (4%)	0.68
CHADS2-score	1.0 (0–2)	1 (0–2)	1 (0–2)	0.11	1 (0–2)	1 (0–2)	0.11
0	60 (28%)	27 (25%)	33 (31%)		29 (30%)	27 (27%)	
1	81 (38%)	38 (35%)	43 (40%)	0.23	37 (38%)	40 (40%)	0.90
2–5	72 (34%)	42 (39%)	30 (28%)		31 (32%)	33 (33%)	
Medication							
Acenocoumarol	195 (91%)	106 (98%)	89 (83%)	<0.001	92 (94%)	87 (86%)	0.10
Anti-arrhythmic drug (any)	48 (22%)	21 (19%)	27 (25%)	0.41	15 (15%)	29 (29%)	0.027
Sotalol	28 (13%)	15 (14%)	13 (12%)	0.84	13 (13%)	14 (14%)	1.00
Amiodarone	14 (7%)	5 (5%)	9 (8%)	0.28	2 (2%)	9 (9%)	0.06
Flecainide	8 (4%)	2 (2%)	6 (6%)	0.28	1 (1%)	7 (7%)	0.07
Betablocker	153 (71%)	78 (72%)	75 (70%)	0.76	71 (72%)	70 (69%)	0.64
Verapamil	13 (6%)	6 (6%)	7 (6%)	1.00	3 (3%)	9 (9%)	0.14
Digoxin	50 (23%)	33 (31%)	17 (16%)	0.015	26 (27%)	20 (20%)	0.31
ACE-i/ATII-antagonist	139 (65%)	77 (71%)	62 (58%)	0.025	64 (65%)	66 (65%)	1.00
Statin	102 (47%)	51 (47%)	51 (48%)	1.00	44 (45%)	48 (48%)	0.78
Echocardiographic parameters							
Frame rate (frames/s)	101 (94–104)	99 (75–104)	101 (97–104)	0.043	101 (94–104)	101 (94–103)	0.67
Heart rate (b.p.m.)	81 (74–96)	79 (72–88)	85 (76–102)	0.005	82 (72–94)	83 (75–100)	0.26
LV ejection fraction (%)	54 (44–60)	52 (42–59)	55 (46–61)	0.07	50 (41–58)	56 (47–63)	0.001
LA diameter (mm)	45 (41–48)	45 (42–49)	44 (41–48)	0.14	45 (41–48)	45 (42–49)	0.39
LA volume (cc)	90 (71–108)	89 (67–107)	91 (76–111)	0.22	88 (68–107)	96 (75–113)	0.14
LA volume index (mL/m^2)	44 (37–54)	43 (35–52)	45 (37–55)	0.32	42 (34–50)	47 (38–58)	0.031
RA volume (cc)	71 (54–93)	73 (55–96)	70 (52–90)	0.41	77 (57–97)	70 (54–93)	0.19
LVEDD (mm)	50 (46–54)	50 (45–55)	51 (47–54)	0.23	50 (47–55)	50 (46–54)	0.69
LVESD (mm)	35 (31–41)	35 (31–43)	36 (32–40)	0.92	36 (32–42)	35 (31–41)	0.24
IVSEDWT (mm)	10 (9–10)	10 (9–10)	9 (9–10)	0.017	10 (9–10)	9 (8–10)	0.12
PWEDWT (mm)	9 (9–10)	10 (9–10)	9 (8–10)	0.041	9 (9–10)	9 (8–10)	0.16

Results are shown as number (%) or as median (interquartile range).
ACE-i, angiotensin-converting enzyme inhibitors; AFCL, atrial fibrillatory cycle length; AFV, atrial fibrillatory wall velocity; ARB, angiotensin II receptor blocker; COPD, chronic obstructive pulmonary disease; IVSEDWT, interventricular septal end-diastolic wall thickness; LA, left atrial; LV, left ventricular; LVEDD, LV end-diastolic dimension; LVESD, LV end-systolic dimension; PWEDWT, posterior wall end-diastolic wall thickness; RA, right atrial; TIA, transient ischaemic attack; TVI, tissue velocity imaging.

Table 2 Multivariate linear regression assessing independent clinical and echocardiographic determinants of AFV-TVI and AFCL-TVI

	Univariate			Multivariate		
	B	95% CI for (*B*)	*P*-value	*B*	95% CI for (*B*)	*P*-value
Determinants of AFV-TVI						
Duration AF episode (per month)	−0.05	−0.8 to −0.24	<0.001	−0.035	−0.062 to −0.008	0.010
LV ejection fraction (per 10%)	0.10	−0.03 to 0.22	0.12			
IVSEDWT (mm)	−0.04	−0.12 to −0.05	0.43			
PWEDWT (mm)	−0.06	−0.19 to −0.06	0.33			
Significant mitral valve regurgitation (≥grade 2)	−0.61	−0.98 to −0.24	0.001	−0.405	−0.772 to −0.038	0.031
Heart rate (b.p.m.)	0.017	0.009–0.025	< 0.001	0.013	0.005 to 0.021	0.002
Determinants of AFCL-TVI						
Duration AF episode (per month)	−0.004	−0.009–0.002	0.18			
LV ejection fraction (per 10%)	0.03	0.009–0.056	0.007	0.038	0.013–0.064	0.004
Gender	0.05	−0.019–0.109	0.17			
LA volume index (per 10 mL/m^2)	0.019	−0.002–0.040	0.07	0.024	0.003–0.044	0.023

AFCL, atrial fibrillatory cycle length; AFV, atrial fibrillatory wall velocity; IVSEDWT, interventricular septal end-diastolic wall thickness; LA, left atrial; LV, left ventricular; PWEDWT, posterior wall end-diastolic wall thickness; TVI, tissue velocity imaging.

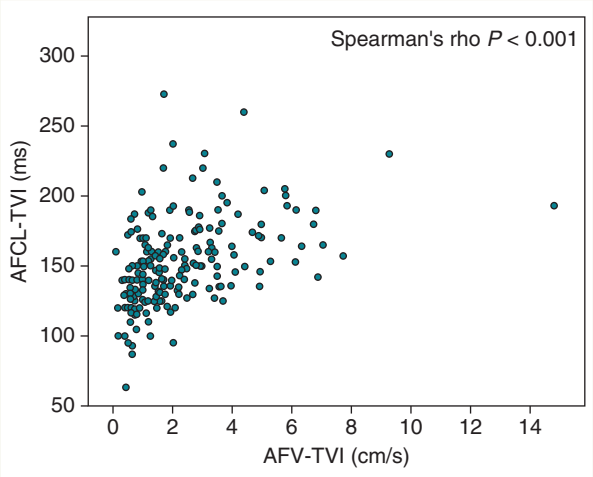


Figure 2 Relationship between AFCL and AFV.

significant mitral valve regurgitation. In addition, AFCL-TVI representing atrial fibrillatory cycle length is related to LA volume index and LV ejection fraction, with lower LA volume index and lower ejection fraction being significantly associated with shorter cycle length. These associations between atrial TVI parameters and clinical correlates were found independent from conventional echocardiographic parameters or clinical parameters including age, hypertension, heart failure, and other constituents of the $CHADS_2$ score including the $CHADS_2$ score itself. Hence, AFV-TVI and AFCL-TVI, both associated with atrial remodelling, are new tools which permit to study atrial remodelling in a non-invasive way.

Determinants of atrial fibrillation wall motion velocity measured with tissue velocity imaging

Atrial fibrosis is an important hallmark of arrhythmogenic remodelling.[15] On echocardiographic TVI it will show as a decreased atrial contractility resulting in lower atrial fibrillatory wall velocities.[6] A low wall velocity may also reflect an increased complexity of fibrillatory conduction associated with a high number of fibrillation waves resulting in multiple but small areas of the atrial myocardium undergoing contraction or relaxation.[16–19] The multivariate analysis revealed that each additional month of AF duration of the current episode decreases the AFV-TVI with ∼0.04 cm/s, the presence of mitral valve regurgitation grade 2 or more decreases the AFV-TVI with ∼0.41 cm/s and every beat per minute increases the AFV-TVI with ∼0.01. One could expect the inverse relationship between AFV-TVI and duration of AF since lower atrial wall velocities are associated with permanent AF as shown by De Vos *et al.*[6] The association can be explained by the presence of fragmentation in patients with longer existing AF.[6] Fragmentation is associated with fibrosis which promotes persistence of the arrhythmia. These factors contribute to a decreased atrial contractility which results in a lower atrial wall velocity.

In addition, the presence of a severe mitral valve regurgitation was also associated with a lower AFV-TVI, with a reverse linear relation between the severity of MR and AFV-TVI. Moreover, patients with MR showed more frequently a non-contractile atrium. Cameli *et al.*[20] showed—using speckle tracking echocardiography—that global peak atrial longitudinal strain was progressively impaired moving from moderate to severe MR. Both, the impaired strain and the lower AFV-TVI could be explained by loss of myocytes and left atrial fibrosis caused by mitral valve

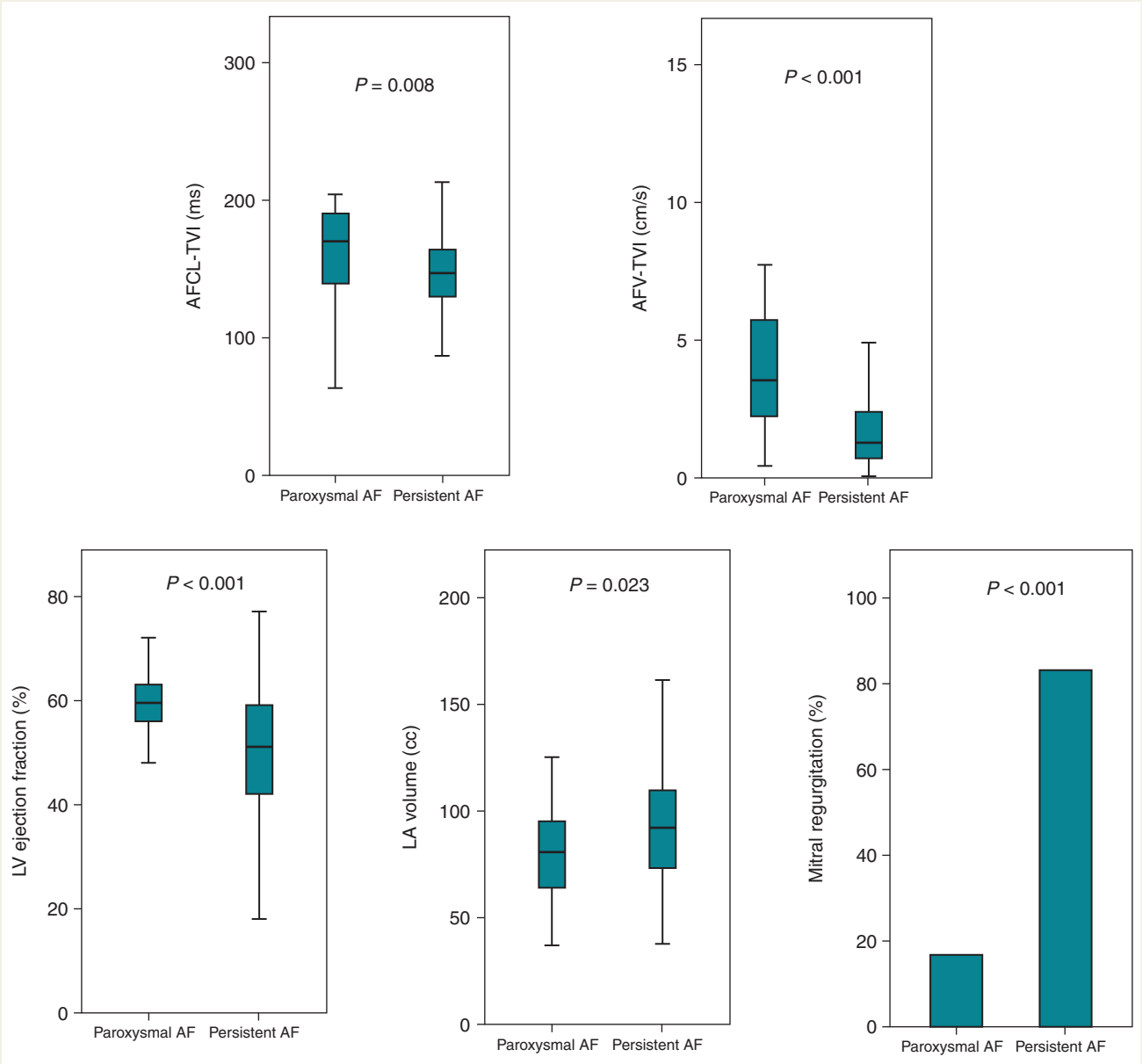


Figure 3 Patients with PAF vs. persistent AF. Boxplots presenting AFCL-TVI, AFV-TVI, LV ejection fraction, and LA volume per type of AF. Bar graph presenting % of MR per type of AF.

disease-related atrial pressure overload and enlargement. Interestingly, the relationship between MR severity and atrial contractility was not seen with LA volume or volume index. This suggests that contractility changes as represented by AFV-TVI may precede atrial volume changes. Although not significant, the opposite was found concerning the AFCL-TVI, i.e. the more severe the mitral valve regurgitation, the longer the AFCL-TVI (data not shown). This is in agreement with the study of Tieleman who showed that effective refractory period (ERP) was prolonged in patients with mitral valve regurgitation compared with patients without this condition.[21] Thus, TVI parameters may be promising tools for early assessment of severity of MR in patients with persistent AF.

A high AFV-TVI was associated with higher ventricular rate, which is difficult to explain. It may, e.g. relate to relatively healthy atria allowing for unhampered atrioventricular conduction of the atrial impulses. Likewise, a relatively high heart rate may represent a higher autonomic tone producing both higher heart rate and increased AFV-TVI as a marker of atrial contractility. Notwithstanding these possible explanations, it is difficult to tell whether this finding is clinically relevant.

Although not significant, in our population there was a trend towards a higher prevalence of ischaemic stroke or TIA in the medical history in the group who had a low AFV-TVI (11 vs. 5% of the patients). A low AFV-TVI, represents decreased contractility which may enhance blood stasis and risk for thromboembolism.

Up till now left atrial size and function have not been incorporated in stroke risk prediction rules like the CHA_2DS_2-VASc score, simply because atrial abnormalities are considered a marker for other thrombogenic conditions. This suggests that size and function are too distant from essential pathophysiological mechanisms related to atrial thrombogenesis and stroke.[11] Currently, transoesophageal echocardiography is the gold standard for the detection of thrombi in the LA.[22] Unfortunately, it is semi-invasive and patient-unfriendly and therefore it has never gained a large role in fine tuning stroke risk in patients with AF.[23,24] Transthoracic assessment of LA function using speckle tracking has recently gained more and more interest with respect to studying stroke mechanisms and predicting stroke risk.[25–27] Taken together, we believe that stroke risk assessment can be fine tuned if easy-to-obtain echocardiography data like atrial size and function—including AFV-TVI assessment—are used systematically. Hopefully future studies will incorporate relevant echocardiographic data points including parameters like AFV-TVI for assessment of stroke risk in patients with AF. Patients with a lower AFV-TVI also had LVH which would suggest the presence of more structural remodelling in patients with LVH. Recently, Akkaya *et al.*[28] showed using MRI that patients with LVH have a greater degree of left atrial structural remodelling compared with patients without LVH. The left atrial remodelling is triggered by the left atrial wall stretch as a consequence of higher pressure in the LV and LA. Multivariately, LVH was not related to AFV-TVI.

Determinants of atrial fibrillation cycle length determined by tissue velocity imaging

In experimental studies, changes in atrial contractile function and fibrillatory cycle length during ongoing AF go hand in hand.[29] This was also seen in the present study (*Figure 2*). Atrial fibrillation duration was univariately related with the AFCL-TVI and patients with PAF had a significantly shorter AFCL-TVI compared with patients with persistent AF. This is in agreement with an electrophysiological study which showed that patients with persistent AF had significantly shorter atrial ERPs, here represented by AFCL-TVI, compared with patients with PAF.[30] De Vos *et al.*[6] also found that the AFCL-TVI and the AFV-TVI were related to the type of AF. However, multivariately AF duration was not associated with AFCL-TVI, possibly caused by the low number of study patients. Multivariate analysis revealed only LVEF and indexed left atrial volume (LAVI) as independent determinants of AFCL-TVI. Each additional 10% LVEF increases the AFCL-TVI with 0.03 ms and each 10 mL/m^2 LAVI increases the AFCL-TVI with 0.02 ms. The difference in LVEF was small, yet significant with a higher LVEF being associated with a longer AFCL-TVI. Possibly a reduced LV systolic function causes atrial stretch which results in atrial conduction abnormalities. However, results from other studies are inconsistent. Animal studies have shown that heart failure causes interstitial fibrosis without reducing the atrial ERP[31] and Sanders *et al.*[32] even found an increase in ERP. This finding is in agreement with a study of Akkaya *et al.*[33] who evaluated the degree of structural LA remodelling using MRI in pre-ablation patients. They concluded that patients with LV systolic dysfunction (cut-off point LVEF 50%) displayed more LA structural remodelling than patients with normal LVEF. This could also result in a shorter AFCL since it reflects electrical remodelling which is shown to be closely related to structural remodelling.[29] Secondly, an increase of LAVI was related to a longer AFCL-TVI. Previous studies have shown that an enlarged atrium is associated with lengthening of the atrial refractory period and fibrillatory cycle length thus counteracting the cycle length shortening caused by AF itself.[21,34,35] Similarly, in dilated atria significantly less shortening of the AFCL occurs than in non-dilated atria.[36]

Limitations

Currently, measuring the TVI parameters in patients with a high ventricular rate is not feasible. The mean heart rate of these excluded patients was 104 ± 23 b.p.m. compared with 86 ± 18 b.p.m. in patients who were included for further analysis in this study. For adequate measurement of the TVI parameters, a long diastole is needed to avoid artefacts by ventricular motion. Unless a patient with a high ventricular rate has incidental pauses long enough for TVI measurements, we propose a cut-off heart rate below 100 b.p.m. for adequate TVI measurement. To obtain a low enough heart rate, patients need to rest before the echocardiogram is taken. Alternatively, rate control drugs may be administered to obtain sufficiently long diastole but such manoeuvres may limit feasibility of the measurements in clinical practice. A higher frame rate could improve the quality of the TVI measurement. In addition, further studies are required to evaluate the added value of measuring velocities in the parasternal axis. No detailed data were available regarding the valvular disease because this was a retrospective study. Further studies focusing on the relationship between TVI parameters and valvular disease, especially mitral valve disease, are needed.

Clinical implications

Non-invasive assessment of the atrial substrate in patients with AF is challenging. Such assessment—if robust—may broaden our understanding of AF, guide therapy, and help assess arrhythmia prognosis and stroke risk in patients with AF. We and others have shown that electro-echocardiographic total atrial activation time measured during sinus rhythm may predict incident AF in high-risk subjects.[37–39] A very attractive imaging modality of the atrial scene of calamity is through cardiac MRI delayed enhancement of the atrial wall.[40,41] Unfortunately, its way into clinical practice is hampered by limited resolution. Considering the current findings, we feel that direct atrial contractility measurement using TVI might be a promising predictive tool beyond other echo parameters since it associates with important clinical parameters. In particular, atrial TVI parameters as presented herein may be used to validate a diagnosis of recent onset AF (if high AFV-TVI) in patients with unknown AF duration. Finally, AFCL-TVI may reflect significant arrhythmogenic shortening of the atrial refractory period despite relatively normal atrial size. Further studies are needed to evaluate whether the transthoracic AFV-TVI parameter can reliably identify patients at risk for stroke.

Conclusion

This study investigated the clinical and echocardiographic correlates of atrial remodelling assessed by TVI. The atrial fibrillatory velocity is reduced in patients with long AF duration and patients with mitral

valve regurgitation. In addition, atrial fibrillatory cycle length is long if atrial volume index is high and ejection fraction preserved. Atrial TVI parameters measured during AF may be helpful to characterize atrial remodelling and optimize treatment.

Acknowledgements

The authors thank Sandra Sanders-van Wijk, MD for assistance with statistical analyses.

Conflict of interest: none declared.

Funding

This work was supported by NHF grant number 2010B275, European Network for Translational Research in AF (FP7 collaborative project EUTRAF, No. 261057). I.L. was supported by grant NHF 2010B275.

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