The mitral late diastolic flow acceleration slope after the restoration of sinus rhythm in acute atrial fibrillation: relationship to atrial function and change over time

Akut atriyal fibrilasyonda sinüs ritmi elde edildikten sonra mitral geç diyastolik akım akselerasyon eğimi: Atriyal fonksiyonla ilişkisi ve zamanla değişimi

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ABSTRACT

Objective: This study was prospectively designed to evaluate the relationship between the mitral A wave acceleration slope (AWA-slope) and the left atrial ejection fraction (LA-EF) after the restoration of sinus rhythm in patients with atrial fibrillation (AF), and also to evaluate the change in the AWA-slope between the sequent second day and first month.

Methods: Twenty-nine patients (16 female, mean age 56±13 years) with unknown cause of AF (except for age) converted to sinus rhythm within the first 48 hours were included into the study. A transthoracic echocardiography was performed in all patients on the second day and the first month after restoration of the sinus rhythm. The paired Student's t test was used in comparisons of the continuous variables. The simple and multiple correlations of the LA-EF were evaluated by the simple and multiple linear regression analyses, respectively.

Results: Left atrial ejection fraction (42±17 vs 51±19%, p=0.03) and AWA-slope (950±337 vs 1087±351 cm/sec^2, p=0.021) obtained after the first month were greater than on the second day. A significant correlation between LA-EF and AWA-slope was observed both on the second day (r=0.76, p<0.001) and at the end of the first month (r=0.71, p<0.001). In addition, there were the correlations between LA-EF and mitral A wave peak velocity (r=0.42, p=0.025) or mitral E/A ratio (r=-0.39, p=0.040) at the end of the first month. On multiple linear regression analysis, only AWA-slope was found to be related to LA-EF (y=9.35+0.04 (AWA-slope), the overall R^2=0.51, beta =0.71; 95% CI 0.02-0.05; p<0.001).

Conclusion: Mitral A wave acceleration slope is a simple, reliable and non-invasive method that can be used to evaluate left atrial contractile function. It can also be used in monitoring of atrial stunning period in patients with sinus rhythm converted from AF.

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Key words: Atrial function, atrial fibrillation, mitral A wave acceleration slope, left atrial ejection fraction

ÖZET

Amaç: Bu çalışma, atriyal fibrilasyonlu (AF) hastalarda sinüs ritmi elde edildikten sonra mitral A dalga akselerasyon eğimi (ADA-eğimi) ile sol atriyal ejeksiyon fraksiyonu (SA-EF) arasındaki ilişkiyi ve 2. gün ile 1. ay arasında ADA-eğimindeki değişimi değerlendirmek için prospektif olarak düzenlendi.

Yöntemler: Yaş haricinde bir sebep bulunamayan ve ilk 48 saat içinde sinus ritmine döndürülen AF'li 16'sı bayan 29 hasta (16 bayan, ortalama yaş 56±13 yıl) çalışmaya alındı. Transtorasik ekokardiyografi sinüs ritmi elde edildikten sonraki 2. gün ve 1. ayda bütün hastalara uygulandı. Sayısal değişkenlerin karşılaştırılmasında eşlenmiş Student-t testi kullanıldı. Sol atriyal ejeksiyon fraksiyonunun tekli ve çoklu korelasyonları sırasıyla basit ve çoklu lineer regresyon analizleri ile değerlendirildi.

Bulgular: Sol atriyal ejeksiyon fraksiyonu (%51±19'a karşı %42±17, p=0.03) ve ADA-eğimi (1087±351'e karşı 950±337cm/sn^2, p=0.021) 1. ayda 2. güne göre daha büyük idi. Hem 2. günde ve hem de 1. ayda SA-EF ile ADA-eğimi arasında anlamlı korelasyon gözlendi (sırasıyla r=0.76, p<0.001 ve r=0.71, p<0.001). Ayrıca 1. aydaki SA-EF ile mitral A dalga pik hızı (r=0.42, p=0.025) ve mitral E/A oranı (r=-0.39, p=0.040) arasında da anlamlı korelasyonlar bulundu. Çoklu lineer regresyon analizinde, sadece ADA-eğimi SA-EF ile ilişkili bulundu [=9.35+0.04 (ADA-eğimi), R^2=0.51, beta katsayısı=0.71 (%95 güvenlik aralığı 0.02-0.05) ve p<0.001].

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Sonuç: Mitral A dalga akselerasyon eğimi sol atriyal kontraktil fonksiyonunu değerlendirmek için kullanılabilecek basit, güvenilebilir ve invazif olmayan bir yöntemdir. Aynı zamanda AF'den sinüs ritmine döndürülen hastalarda atriyal 'stunning' dönemini izlemede de kullanılabilir.
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Anahtar kelimeler: Atriyal fonksiyon, atriyal fibrilasyon, mitral A dalga akselerasyon eğimi, sol atriyal ejeksiyon fraksiyonu

Introduction

Atrial fibrillation (AF) is characterized by a lack of organized electrical and mechanical atrial activity. The estimated prevalence of AF is 0.4% to 1% in the general population, increasing with age and it is the most commonly encountered arrhythmia in clinical practice (1, 2). Atrial fibrillation has a high rate of morbidity and mortality. Although it is frequently associated with cardiac disease, systemic hypertension, diabetes mellitus and pulmonary diseases, AF may appear with rates changing between 2.7% and 30% as well (3-5).

In the presence of AF, the atrial contribution to the ventricular filling is lost, while the risk for systemic and pulmonary embolism increases due to blood stasis in the atria. Therefore, the sinus rhythm in patients with AF should be restored. Sinus rhythm in these patients can be restored spontaneously, as well as by electrical or pharmacological cardioversion. However, late embolism has been reported several days to weeks after a successful cardioversion in patients who have maintained sinus rhythm (6-9). Transesophageal studies have shown that a new or denser spontaneous echo-contrast is developed within the left atrium after successful cardioversion (10, 11). It has been reported a period called as "atrial stunning", that atrial contraction has not been developed despite the restoration of electrical activity after cardioversion (8, 12, 13). The duration of this period is associated with the duration of AF before cardioversion (14, 15).

Many invasive (16-18) and noninvasive (19-22) methods have been suggested for evaluating the contractile function of the left atrium. While the invasive methods are based on a pressure-volume relationship that is taken simultaneously (16, 17), noninvasive methods are generated from either the left atrial volumes (LAVs) (10, 23) or mitral flow Doppler data (15, 19, 24). The left atrial dP/dt, one of the invasive methods, was obtained from the left atrial pressure trace by copying that of the left ventricle (18, 19). The acceleration slope of the mitral late diastolic flow Doppler trace (A Wave Acceleration slope=AWA-slope) is obtained as a function of velocity, which is the marker of pressure on the y-axis, with time being on the x-axis. It has been reported that the AWA-slope might be a noninvasive indicator of the invasive left atrial dP/dt (19). However, this relationship was not based on the simultaneous data. Therefore, it has not been known that the relation between the AWA-slope and the contractile function of the left atrium, which was simultaneously obtained by echocardiography.

This study was prospectively planned to evaluate the relationship between the AWA-slope and the left atrial ejection fraction (LA-EF) after the restoration of sinus rhythm in patients with acute AF without any cause, and also to evaluate the change in the AWA-slope between the sequent second day and first month.

Methods

Study population and protocol

The study was designed as retrospective analysis of prospective cohort data. Patients with AF that presented to our emergency department between January 2000 and December 2001, who did not have any known cardiovascular or systemic disease and who was converted to sinus rhythm within the first 48 hours were included in the study. Patients who had moderate to severe valvular heart disease, left ventricular dilatation, left ventricular hypertrophy, a diastolic filling impairment that was worse than abnormal relaxation, insufficient echo-images, bundle branch block, frequent premature beats or high blood pressure in the first echocardiographic examination were excluded from the study. In addition, patients in whom a cause (other than age) for AF could be determined or in whom AF was repeated during a one-month follow-up period after the restoration of sinus rhythm were also excluded. On this basis, the study was performed with data attained from 29 patients. All of the patients were taking antiarrhythmic and anticoagulant therapy. Transthoracic echocardiography was performed on the day after the first 24 hours and the first month subsequent to the restoration of the sinus rhythm. All of the patients had diagnostic tests for AF within one month. The patients were given information about the study and their consent was obtained. The approval of the Internal Review Boards was taken.

Echocardiographic study

Transthoracic echocardiography was performed using a Hewlett-Packard Sonos 1500 instrument (Philips Corporation, Andover, Massachusetts, USA) with a 2.5 or 3.5 MHz phased array transducer. The recordings were taken from patients positioned in the left lateral decubitus position. Simultaneous electrocardiographic recordings were also taken. M-mode traces were recorded at a speed of 50 mm/sec and the Doppler signals were recorded at 100 mm/sec. Three consecutive cycles were averaged for every parameter. Echocardiographic records were videotaped for further analysis.

The left ventricular diameters, left ventricular ejection fraction and left atrial anteroposterior diameter were also determined from M-mode traces that had been recorded from the parasternal long axis view, according to established standards (25). The LAVs were obtained according to the biapical modified Simpson's rule (26). The left atrial volumes measured included the largest

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LAV at the end of ventricular systole (LAV_{max}), the smallest LAV after atrial emptying at the end of ventricular diastole (LAV_{min}) and the LAV at the onset of atrial emptying coincided with pre-p wave on the electrocardiography (LAV_{pre-pw}) (23,27). The left atrial active emptying volume (LAV_{AE}) and the LA-EF were calculated according to the following formulas (23, 27, 28):

$$LAV_{AE} = (LAV_{pre-pw})-(LAV_{min}) \quad (1)$$

$$LA\text{-}EF = (LAV_{AE})/(LAV_{pre-pw}) \quad (2)$$

The pulsed Doppler transmitral inflow tracing was recorded from the apical four-chamber view with the sample volume being positioned between the tips of the mitral leaflets. The mitral A wave acceleration slope was measured from the ascending arm of the pulsed Doppler transmitral late inflow (A wave) tracing (Fig. 1).

Statistical analysis

The SPSS 16.0 program for Windows (SPSS Inc, Chicago, Illinois, USA) was used for all statistical calculations. Numeric values are given as mean±1 standard deviation. The paired Student's t test was used to compare parameters between the second day and the first month after the restoration of sinus rhythm. The changes in the LA-EF and the AWA-slope between the second day and the first month were described as the ratio of the difference between the first month and the second day to that of the second day. The relationship between the changes in both parameters was evaluated with a simple linear regression analysis. Simple linear regression and multiple stepwise (forwards and backwards) linear regression analyses were used to evaluate the correlations between the LA-EF and various clinical and echocardiographic variables. The multivariate model consisted of the LA-EF as the dependent variable and of independent variables that had a significant correlation with the LA-EF in the simple linear regression analysis. Thus, the AWA-slope, the mitral A wave and the mitral E/A ratio were included in the multiple linear regression analysis as the independent variables. The intra and inter-observer variabilities of the AWA-slope measurements were evaluated with simple linear regression and Bland-Altman analyses by using the videotape recordings. A probability value of $p<0.05$ was considered significant and two tailed p values were used for all statistics.

Results

Of the 29 study patients, 16 were female and the mean age was 56±13 years (range 27-81). Atrial fibrillation was recurrent in 20 patients and the first attack in 9 patients. Sinus rhythm was restored with 200 joule DC cardioversion in 1 (3%) patient, with pharmacological cardioversion in 24 (83%) patients, and spontaneously in 4 (14%) patients. Pharmacological cardioversion was accomplished by propafenone in 20 patients, amiodarone in 2 patients and quinidine in 2 patients.

There was no difference between the heart rates measured on the second day and after the first month subsequent to the restoration of sinus rhythm (77±10 versus 73±10 bpm, $p>0.05$). Significant differences were not observed between the second day and the first month in terms of echocardiographic left ventricular diastolic and systolic diameters, the left atrial diameter and the LAV_{max} (Table 1). The LA- EF (42±17% versus 51±19%, $p=0.03$, Fig. 2A), the AWA-slope (950±337 versus 1087±351 cm/sec^2, $p=0.021$, Fig. 2B) and the mitral A wave peak velocity (70±14 versus 76±19 cm/sec, $p=0.024$) were greater in the first month compared to the second day.

A significant correlation between the LA-EF and the AWA-slope were observed both on the second day ($r=0.76$, $p<0.001$,

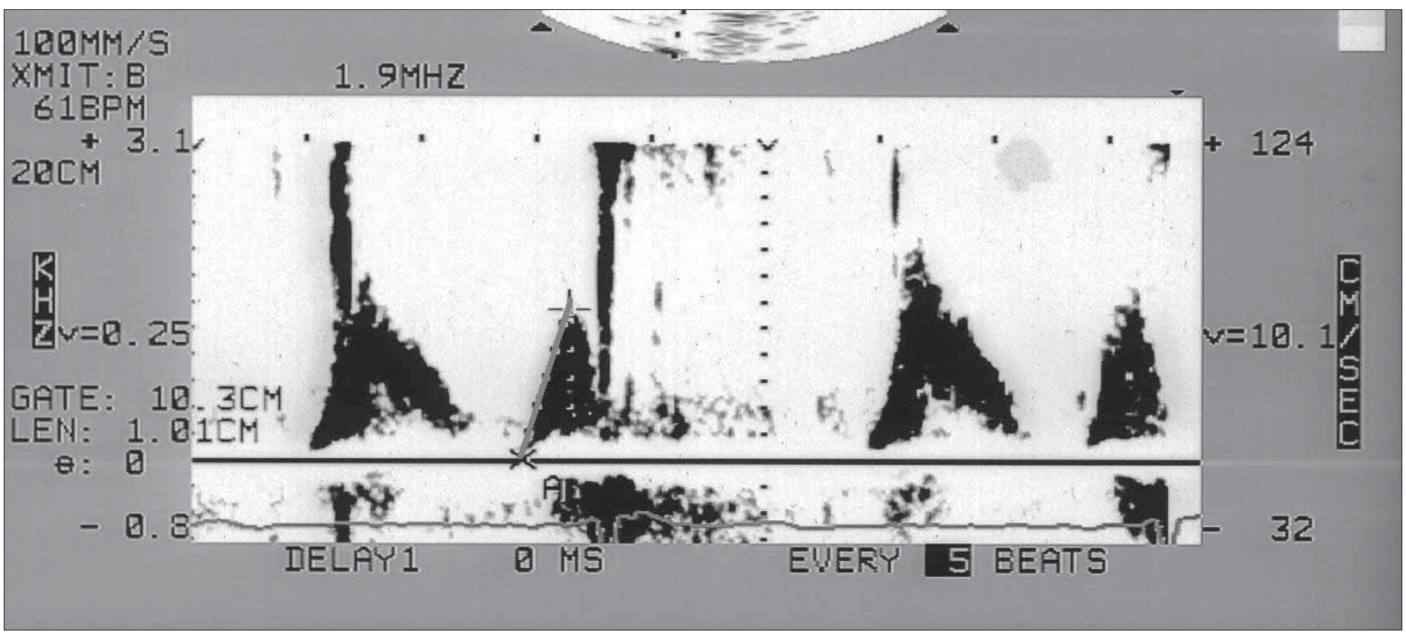

Figure 1. The measurement of the mitral A wave acceleration slope (AWA-slope). The grey line shows the measurement of the AWA-slope (from base to peak of mitral A wave Doppler tracing)

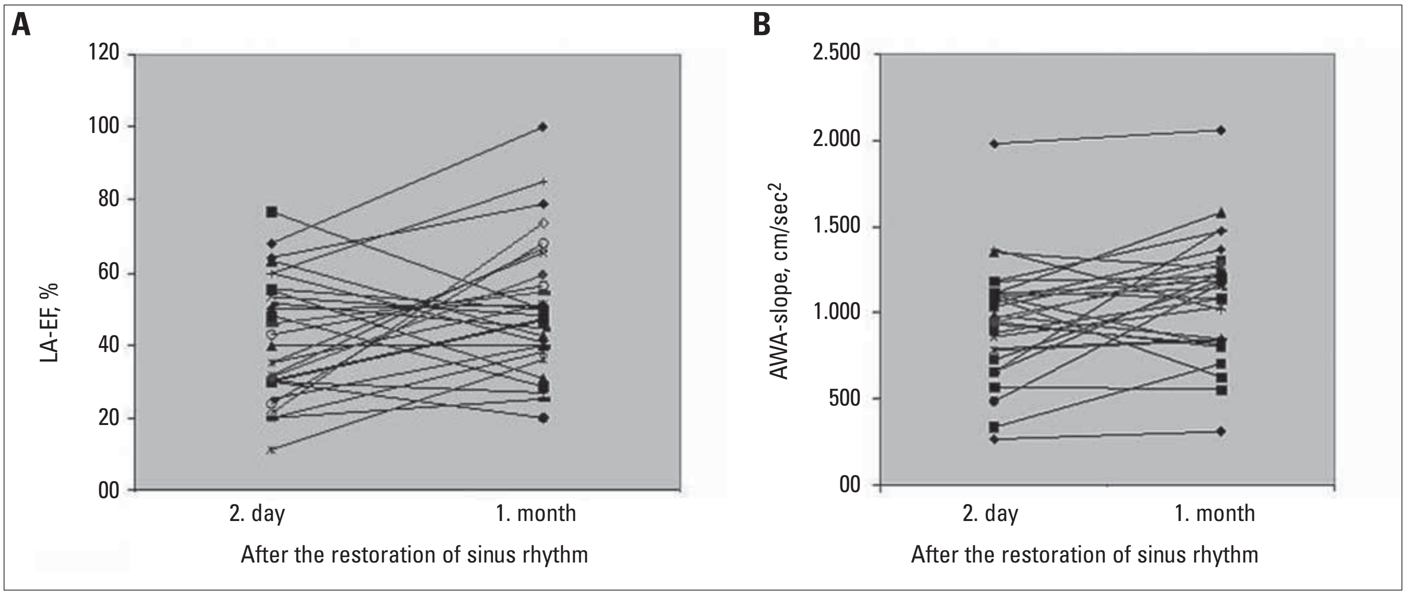

Figure 2. Distributions of the left atrial ejection fraction (LA-EF) (A) and the mitral A wave acceleration slope (AWA-slope) (B) on 2nd day and after the 1st month subsequent to the restoration of sinus rhythm

Table 1. Comparison of echocardiographic parameters of patients obtained on the 2nd day and after the 1st month subsequent to restoration of sinus rhythm

Variables	2nd day	1st month	p*
Heart rate, bpm	77±10	73±10	NS
LVDd, mm	45±5	47±6	NS
LVSd, mm	28±6	30±5	NS
EF, %	68±11	67±7	NS
LAd-AP, mm	37±8	37±6	NS
LAVmax, cm^3	52±37	50±25	NS
LAVmin, cm^3	18±10	17±13	NS
LAVpre-pw, cm^3	35±22	39±23	NS
LA-EF, %	42±17	51±19	0.030
A-wave peak velocity, cm/sec	70±14	76±19	0.024
E/A ratio	1.09±0.34	1.05±0.50	NS
AWA-slope, cm/sec^2	950±337	1087±351	0.021

Data are presented as mean±1 standard deviation
*paired Student's t test
AWA-slope - mitral A wave acceleration slope, E/A - the ratio of mitral diastolic early to late flow velocities, EF - left ventricular ejection fraction, LAd-AP - left atrial antero-posterior diameter, LA-EF - left atrial ejection fraction, LAV_{max} - the largest left atrial volume at the end of ventricular systole, LAV_{min} - the smallest left atrial volume after atrial emptying at the end of ventricular diastole, LAV_{pre-pw} - the left atrial volume at the onset of atrial emptying coincided with pre-p wave on electrocardiography, LVDd - left ventricular diastolic diameter; LVSd - left ventricular systolic diameter; NS - non-significant (p>0.05)

Fig. 3A) and after the first month (r=0.71, p<0.001, Fig. 3B). In addition, the LA-EF correlated with the mitral A wave peak velocity (r=0.39, p=0.037; r=0.42, p=0.025; respectively) and the mitral E/A ratio (r=-0.48, p=0.008; r=-0.39, p=0.040; respectively) both on second day and in the first month (Table 2). In the multiple linear regression analysis, the AWA-slope was found to be the parameter most closely related to the LA-EF both on second day [=5.7±0.04 (AWA-slope), the overall R^2=0.57, beta coefficient=0.76 (95% CI 0.03-0.05) and p<0.001] and in the first month [=9.35+0.04 (AWA-slope), the overall R^2=0.51, beta coefficient=0.71 (95% CI 0.02-0.05) and p<0.001]. There was also a significant correlation between the changes in the LA-EF and the AWA-slope from the second day to the first month (r=0.76, p<0.001).

There were excellent intra and inter-observer agreements on the measurement of the AWA-slope (r=0.99, p<0.001; mean difference 2±57 cm/sec^2, SEE 10 cm/sec^2, p=0.84 and r=0.99, p<0.001, mean difference -5±55 cm/sec^2, SEE 10 cm/ sec^2, p=0.60, respectively).

Discussion

The results of the present study show that there is a good correlation between the AWA-slope obtained by Doppler echocardiography and the LA-EF in patients with acute AF that has been restored to sinus rhythm; also there is an increase in the AWA-slope that is in parallel to the increase of the LA-EF after the first month subsequent to the restoration of sinus rhythm.

The validity of the LA-EF as an indicator of atrial contraction: The left atrium modulates left ventricular filling with functions that are performed throughout the cardiac cycle (29). These functions, which have been observed to be three in number, are: 1) reservoir during systole, 2) conduit at early diastole, and 3) active contraction at late diastole (29). While the first two functions are partially affected in patients with AF, atrial contraction completely disappears. Therefore, the atrial contraction in patients who have been converted to sinus rhythm is more observable than other functions.

The contractile function of the left atrium can be most accurately evaluated using an instantaneous pressure-volume relation (16, 17). However, the measurement of this index is technically difficult and too invasive to use in routine clinical practice.

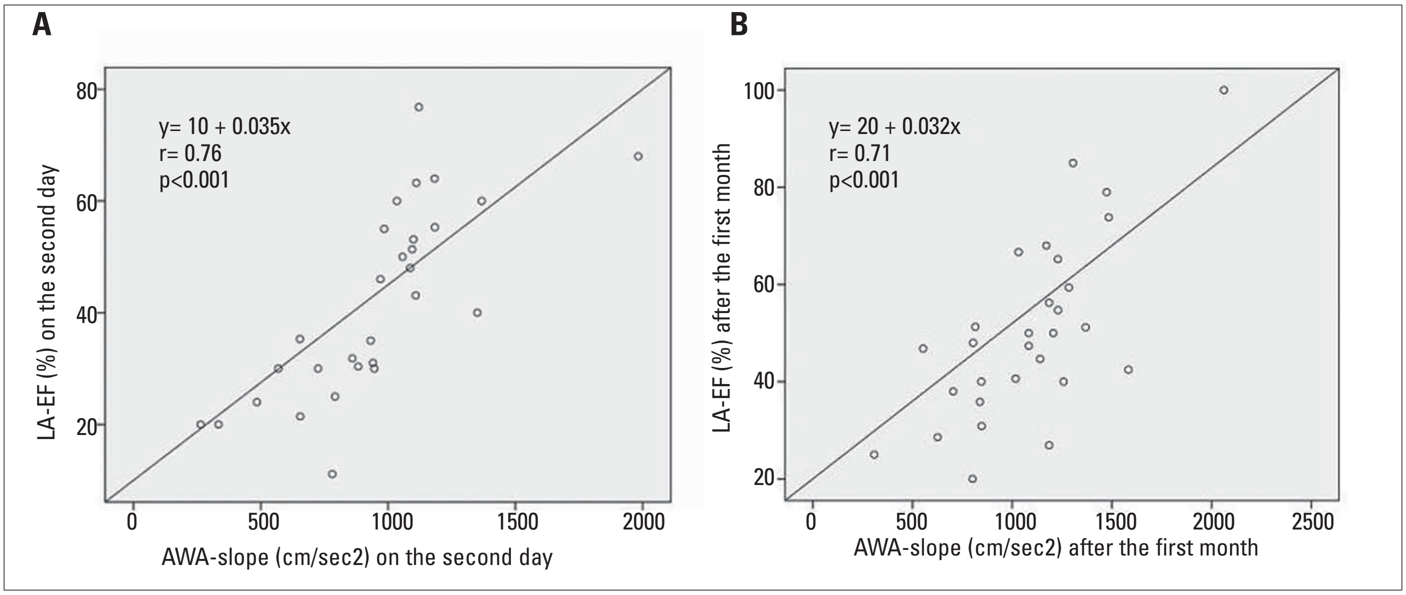

Figure 3. Linear regression curves of the relationship between the left atrial ejection fraction (LA-EF) and the mitral A wave acceleration slope (AWA-slope) on the 2nd day (A) and after the 1st month (B)

Table 2. The correlations between the left atrial ejection fraction and other parameters on 2nd day and after the 1st month subsequent to restoration of sinus rhythm

Variables	On second day		After the first month	
	r	p*	r	p*
Age	-0.03	NS	0.05	NS
Sex	-0.05	NS	0.07	NS
Type of cardioversion	0.24	NS	0.02	NS
Heart rate	0.27	NS	0.05	NS
EF	0.09	NS	0.11	NS
Mitral A-wave peak velocity	0.39	0.037	0.42	0.025
Mitral E/A ratio	-0.48	0.008	-0.39	0.040
AWA-slope	0.76	<0.001	0.71	<0.001

*Simple linear regression analysis
AWA-slope - mitral A wave acceleration slope, E/A - the ratio of mitral diastolic early to late flow velocities, EF - left ventricular ejection fraction, NS - non-significant (p>0.05)

In addition, it is impossible to obtain the instantaneous pressure-volume relation simultaneously with the AWA-slope, which is obtained echocardiographically. Therefore, an echocardiographic method is needed as a reference method to relate the left atrial contraction with the AWA-slope. Echocardiographic methods are derived from either atrial volumes (10, 23) or mitral flow Doppler data (15, 19, 24). As the AWA-slope is obtained from a mitral late diastolic flow Doppler tracing, it can naturally be expected that the AWA-slope is associated with mitral flow-based methods. In the present study, we chose a method that is based on atrial volumes as a reference method to asses the AWA-slope. The atrial volume-based methods are the left atrial active emptying volume or fraction and the LA-EF (23, 28).

The accuracy of left atrium volume measurements used in the reference method might have affected the results of the present study. Studies have shown that there are good correlations between the atrial volume obtained by two-dimensional echocardiography and that obtained by three-dimensional echocardiography (30) or magnetic resonance imaging (31). However, the simultaneous measurements of left atrial volumes with the AWA-slope have increased the accuracy of the present study as the effects of the hemodynamic changes are the same for both parameters.

The relation between the AWA-slope and the LA-EF: The results of the present study show that there is a good positive correlation between the AWA-slope and the LA-EF, that represents the left atrial contractile function. Nakatani et al. (19) reported a similar relationship between left atrium dP/dt that had been obtained invasively and the AWA-slope that had been measured echocardiographically (r=0.78, p<0.001). The AWA-slope, in fact, is a non-invasive measure of the invasively-measured dP/dt. The AWA-slope is calculated by dividing velocity by time in the mitral late diastolic flow Doppler tracing. According to the Bernoulli equation, velocity can be used instead of the pressure gradient between the left atrium and the left ventricle.

During left atrial contraction, the blood in the left atrium flows into both the left ventricle and the pulmonary veins. The AWA-slope is only an indicator of the blood that passes into the left ventricle. If the blood which passes into the pulmonary veins is also taken into account, the correlation with the LA-EF may increase. In fact, Nakatani et al. (19) showed that the correlation between left atrial dP/dt and the AWA-slope combined with the velocity of pulmonary atrial reverse flow was better than that with the AWA-slope alone (r=0.88 vs. r=0.78, respectively). The pulmonary atrial reverse flow is best obtained by transesophageal echocardiography. However, the fact that this is a semi-invasive method limits its routine use.

Another factor that affects the correlation between the AWA-slope and the LA-EF may be the influence of the left ventricular function on mitral late diastolic flow (32). It has been reported that alterations in left ventricular end-diastolic pressure affect the velocity and the time of mitral late diastolic flow (33, 34). Although patients who had a disease that would lead to left ventricular diastolic dysfunction or with moderate to severe impairments in the left ventricular diastolic filling were excluded from the present study, patients with mild diastolic dysfunction could have been included. As left ventricular compliance affects similarly the velocity and the time of mitral late diastolic flow, which are numerator and denominator of AWA-slope, no significant change in the AWA-slope should occur. Therefore, any such interaction of the left ventricular function can be ignored for the present study. However, this should be supported by future studies.

Change in the AWA-slope after the restoration of sinus rhythm: In the present study, the AWA-slope increased after the first month as compared to the second day subsequent to the restoration of sinus rhythm. This increase was parallel to the increase in the LA-EF. These findings are in concordance with the fact of "atrial stunning", which occurs after a successful cardioversion (8, 12, 13). Although the period of atrial stunning is proportional to the duration of AF before cardioversion (15), in 97% of patients, atrial contraction returns to normal within one week (35). The present study is the first to use the AWA-slope to demonstrate improvement in atrial contraction after the restoration of sinus rhythm.

Clinical use of the AWA-slope: The AWA-slope can be used in any situation where the systolic function of the left atrium needs to be evaluated. As in the present study, it can be used to monitor the atrial stunning period after the restoration of sinus rhythm in patients with AF. There is a risk of systemic embolism during this period and the use of an anticoagulant is mandatory. This period may continue for more than one month in some patients. In such a situation, the anticoagulant therapy, which is started empirically and continued for nearly one month should be carried on for a longer duration. The duration of anticoagulation may be determined by the serial follow-up of the AWA-slope. Atrial fibrillation can recur in some patients who have converted to sinus rhythm. In such patients, the risk of an embolism is high. The AWA-slope may be a guide to predict in which patients AF can develop. However, this needs to be demonstrated with further studies.

Left atrial contraction is important in certain diseases. Among these, the leading conditions are valvular heart diseases and left ventricular dysfunction. In addition, the AWA-slope can also be used to evaluate the success of interventions (antiarrhythmic drugs, Maze operation and catheter ablation) performed to convert AF to sinus rhythm. The AWA-slope can be used in the evaluation of the left atrial appendage function (36). It has been reported that the accuracy, sensitivity and specificity of the AWA-slope for demonstrating low left atrial appendage emptying velocity (<56 cm/sec) in patients with an AWA-slope lower than 900 cm/sec^2 were 90%, 92% and 80%, respectively (36).

A number of methods have been suggested in the evaluation of left atrial contractile functions. Among the non-invasive methods available are mitral A wave peak velocity (24), mitral A wave filling fraction (15) and atrial ejection force (21). Although it is easy to measure mitral A wave peak velocity, this can be influenced by heart rate (37), load changes (37), age (38) and left ventricular diastolic function (33). In the present study, it was seen that the relation between the AWA-slope and the LA-EF is independent from heart rate and age. It is difficult to evaluate the correlation between left ventricular diastolic function and the AWA-slope in the present study, as patients with grade 2 and greater diastolic filling impairment were excluded. However, as left ventricular diastolic function has a similar effect on both the mitral A wave peak velocity (33) and time (34), which are the two components of the AWA-slope, it may not have an effect on the AWA-slope. In addition, it has been found in both our study and that of Nakatani et al. (19) that the AWA-slope is more closely related to left atrial contractility than mitral A wave peak velocity. The mitral A wave filling fraction is calculated by dividing the time velocity integral of the mitral A wave by that of the total diastolic transmitral flow (15). This calculation is less practical than the AWA-slope and also reflects the contribution of atrial contraction to ventricular filling rather than the intrinsic characteristic of the left atrial contraction. Atrial ejection force is calculated based on Newtonian principles (21). Since this calculation needs more than one parameter (mitral annulus diameter and mitral A wave peak velocity), the margin of error may increase. In addition, not only is it difficult to measure the mitral annulus diameter accurately, but this also changes throughout the cardiac cycle (39).

Since the ascending arm of mitral A wave is relatively flat, the line drawn between the beginning and the peak of the wave reflects the AWA-slope, thus making it easy to measure. In addition, low inter- and intra-observer variabilities support the clinical use of the AWA-slope.

Conclusion

The AWA-slope is a simple, reliable and non-invasive method that can be used in the evaluation of the left atrial contractile function. These characteristics of the method may make it attractive in evaluating the atrial stunning period as well as in evaluating the need for anticoagulants in AF patients who have been converted to sinus rhythm.

Conflict of interest: None declared.

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