Evaluation of Left Atrial Appendage Functions in Patients with Thrombus and Spontaneous Echo Contrast in Left Atrial Appendage by Using Color Doppler Tissue Imaging

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Objective: Thrombus and spontaneous echo contrast (SEC) develops in the left atrial appendage (LAA) when LAA function is disturbed. Decrease of left atrial appendage emptying velocity shows LAA dysfunction. The purpose of this study is to examine the incidence of SEC and/or thrombus in LAA in patients with acute myocardial infarction and to assess the LAA function using color Doppler tissue imaging (CDTI) of the patients with detected SEC and/or thrombus.

Method and Results: Eighty-four patients with acute myocardial infarction were included in the study. Spontaneous echo contrast and/or thrombus were observed in 24 (29%) of the 84 patients who were categorized as group 1 (mean age 59 ± 12 years). Sixty patients (71%) without thrombus and/or SEC in LAA were categorized as group 2 (mean age 58 ± 8 years). Left atrial diameters and left ventricular ejection fraction were measured by using transthoracic echocardiography. Left atrial appendage emptying and LAA filling velocity were measured by transesophageal Doppler echocardiography. Systolic appendage tissue velocities (SaV cm/s) were measured at the basal, mid, and tip of medial wall of LAA by transesophageal CDTI. Group 1 had significantly decreased LAA emptying velocities, mid SaVs, and left ventricular ejection fractions compared to group 2 (37 ± 9 cm/s vs 55 ± 22 cm/s, 3.1 ± 1.6 cm/s vs 3.7 ± 1.2 cm/s, and $47 \pm 13\%$ vs $58 \pm 10\%$, respectively, $P = 0.002$, $P = 0.04$, $P = 0.03$). Group 1 had significantly increased left atrial diameters compared to group 2 (40 ± 5 mm vs 36 ± 6 mm $P = 0.001$). Left atrial appendage-filling velocities, basal SaVs and tip SaVs in group 1 were lower than those in group 2 but not significantly.

Conclusions: Mid-SaV of LAA medial wall and LAA emptying velocity decrease in patients with thrombus and/or SEC were an indication of functional disorder of LAA. Color Doppler tissue imaging appears to be a clinically applicable and reliable imaging technique that allows quantitative assessment of regional LAA systolic function.

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Color Doppler tissue imaging, left atrial appendage function

Transesophageal echocardiography is the method of choice for evaluating both the structure and function of the left atrial appendage (LAA). Two-dimensional imaging allows detailed information on LAA morphology to be derived in the presence of thrombus and/or spontaneous echo contrast (SEC). Thrombus and/or SEC develop in LAA in patients with LAA dysfunction.^{1–3} Decrease in LAA empty velocity shows LAA dysfunction.⁴ Left ven-

tricular thrombus is usually considered to be the source for embolic events in acute myocardial infarction, but thrombus formation in LAA has been shown in patients with acute myocardial infarction even in the presence of sinus rhythm.⁵ Tissue Doppler echocardiography has increasingly been used to evaluate regional systolic and diastolic functions. Regional systolic functions can be measured by recording regional average systolic myocardial

velocity with real-time color Doppler tissue imaging (CDTI).⁶ We hypothesized that the CDTI measurements could be regionally made in the wall of the LAA considering its muscular structure similar to myocardium.^{7,8} The purpose of this study is to examine the incidence of SEC and/or thrombus in LAA in patients with acute myocardial infarction and to assess the LAA functions using CDTI of the patients with detected SEC and/or thrombus.

METHODS

The study group consisted of 84 patients (65 men, 19 women, mean age 57 ± 11 years) with first acute myocardial infarction. Clinical and demographic characteristics of patients are shown in Table 1. Acute myocardial infarction was diagnosed by typical chest pain lasting for at least 30 minutes, acute ST-T wave changes and characteristic rise and fall of myocardial enzymes. Exclusion criteria were prior myocardial infarction, prior myocardial or valvular heart disease, and atrial fibrillation. During the recruitment period, seven patients were excluded because of poor echocardiographic image quality. All patients gave informed consent, and the study was approved by our institution. Thrombolytic therapy was given to 42 (50%) of the 84 patients. Patients who had thrombolytic therapy received 1.5 million units of streptokinase over a period of 1 hour; which was immediately followed by heparin. Heparin was started with a 5,000 IU bolus followed by continuous infusion to maintain an activated partial thromboplastin time of 1.5 to 2 times control.

Echocardiographic Studies

Transthoracic Echocardiography

In all patients, the echocardiographic examinations were performed after discharge from the Coronary Care Unit within 2 weeks of the acute event (average 7 ± 4 days) when the patients were clinically stable. Patients underwent transthoracic echocardiography Vingmed System V by using 3.5 MHZ probe and tissue harmonic imaging mode when necessary. End-diastolic and end-systolic left ventricular diameter and left atrial diameter were measured from M-mode tracing in the parasternal long-axis view according to standard criteria. Left ventricular ejection fraction was calculated with the modified Simpson's rule.

Transesophageal Echocardiography

Multiplane transesophageal echocardiography was performed by using a 5-MHZ probe.⁹ The LAA was imaged in a basal short-axis view at 40 to 50 degrees. The left atrium and LAA were evaluated for thrombus and SEC. The presence of thrombus was identified when an intracavitary echo-dens mass with an echocardiographic appearance different from the atrial endocardium and the pectinate muscles was detected. Furthermore, special care was taken in differentiating LAA thrombi from other important artifacts, particularly circumflex artery or mitral annular calcification both of which are hyper-refractile. Spontaneous echo contrast was identified when dynamic, swirling intracavitary smoke-like echoes were detected, which

Table 1. Clinical and Demographical Characteristics of Group 1 and Group 2

	Group 1 (with SEC and/or Thrombus) (n = 24)	Group 2 (without SEC and/or Thrombus) (n = 60)
Age (years)	59 ± 12	58 ± 8
Gender (male/female)	20/4	45/15
Hypertension	8 (33%)	28 (39%)
Diabetes mellitus	5 (21%)	6 (10%)
Smoking	15 (63%)	34 (57%)
Total cholesterol level (mg/dl)	211 ± 32	212 ± 42
HDL-cholesterol level (mg/dl)	40 ± 10	36 ± 8
LDL-cholesterol level (mg/dl)	139 ± 29	140 ± 37
Triglyceride level (mg/dl)	211 ± 32	212 ± 42
Myocardial infarction anterior/inferior	21/4	45/15
Left ventricular ejection fraction (%)	$47 \pm 13^*$	58 ± 10

*P = 0.03.

Figure 1. Basal, mid, and tip of medial wall of LAA.

were differentiated from the white noise artifact by their characteristic swirling pattern and by careful attention to the gain settings. Left atrial appendage empty and filling velocities were recorded with pulse wave Doppler while the sample volume was about 1 cm inside of LAA in the same axis.

Left Atrial Appendage Color Tissue Doppler

Color Doppler tissue imaging of the LAA walls during a cardiac cycle was recorded in all patients in the longitudinal view obtaining the color-coded wall dynamics. Sample volume was positioned within the medial walls of the LAA. Color Doppler tissue imaging measurements were taken at basal, mid, and tip of the medial wall of LAA

(Fig. 1). Systolic appendage velocity (SaV) was measured as positive signal (Sa wave) at a point corresponding to the onset of the electrocardiographic P wave (Fig. 2). Measurements of velocities in the LAA were averaged with five consecutive cardiac cycles, and were stored in the clipboard memory of the echo machine. The acquired images were analyzed independently by two blinded cardiologists.

Statistical Analysis

All calculations were performed with an IBM-compatible SPSS (version 10.0) program. All data are presented as mean values with standard deviations ($\pm$ SD). Continuous variables between the two

Figure 2. Systolic appendage velocity (SaV). A positive signal (S wave) is at a point corresponding to the onset of the electrocardiographic P wave. The velocity profile at the tip of left atrial appendage extracted from the color Doppler tissue imaging.

groups were compared by unpaired Student's *t*-test or Mann-Whitney U test. The significance of differences between categorical variables was determined by the chi-square test. A *P* value lesser than 0.05 was considered statistically significant.

RESULTS

Clinical and demographic characteristics of patients are shown in Table 1. Spontaneous echo contrast and/or thrombus in the LAA was found in 24 (28%) patients (SEC in 13 (15%) patients, thrombus and SEC in 11 (13%) patients). In contrast, transthoracic echocardiography failed to demonstrate SEC and/or thrombus in all patients. There was no significant difference between patients treated with (group 1; 13 of 24) and without (group 2; 29 of 60) thrombolytic therapy with regard to the presence of LA thrombus. Patients in group 1 had signif-

icantly decreased LAA emptying velocities, mid-SaVs, and left ventricular ejection fractions compared to group 2 (37 ± 9 cm/s vs 55 ± 22 cm/s, 3.1 ± 1.6 cm/s vs 3.7 ± 1.2 cm/s, and $47 \pm 13\%$ vs $58 \pm 10\%$, respectively, $P = 0.002$, $P = 0.04$, and $P = 0.03$). Patients in group 1 had significantly increased left atrial diameters compared to group 2 (40 ± 5 mm vs 36 ± 6 mm, $P = 0.001$). Left atrial appendage filling velocities, basal SaVs, tip SaVs were lower than in the control group but not significantly ($P = 0.51$, $P = 0.17$, and $P = 0.31$) (see Table 2).

DISCUSSION

Left atrial appendage is a small muscular sac of atrial wall and is a frequent location of SEC and/or thrombus formation in patients with LAA dysfunction. In this study, patients with SEC and/or

Table 2. Echocardiographic Characteristics of Group 1 and Group 2

	Group 1 (with SEC and/or Thrombus) (n = 24)	Group 2 (without SEC and/or Thrombus) (n = 60)	P
LAD (mm)	40 ± 5	36 ± 6	0.001
LAAEV (cm/s)	37 ± 9	55 ± 22	0.002
LAAFV (cm/s)	51 ± 17	52 ± 16	0.51
Basal PSaV (cm/s)	3.3 ± 1	3.7 ± 1.3	0.17
Mid-PSaV(cm/s)	3.1 ± 1.6	3.7 ± 1.2	0.04
Tip PSaV(cm/s)	3.2 ± 1.8	3.6 ± 1.5	0.31

LAD = Left atrial diameter; LAAEV = Left atrial appendage empty velocity; LAAFV = Left atrial appendage filling velocity; PSaV = Peak systolic appendage velocity.

thrombus had a marked LAA contractile dysfunction compared to those without SEC and/or thrombus. We have evaluated the feasibility of CDTI for the assessment of LAA wall movements and described the pattern of LAA systolic velocities (SaV). Mid-SaV of LAA medial wall and LAA emptying velocity decrease in patients with thrombus and/or SEC in the LAA. It has been shown that in patients with severe hypertension and hypertrophic cardiomyopathy in sinus rhythm, a marked elevation in the left atrial pressure reduces the LAA emptying velocities and these changes may be accompanied by an increase in the incidence of thrombus formation in the LAA.^{10–12} Left ventricular systolic and/or diastolic dysfunction may affect LAA contraction, primarily through its effect on LAA filling pressures.¹³ Significant left ventricular dysfunction in sinus rhythm is associated with LAA thrombus formation, and about 15% of patients with severe dilated cardiomyopathy in sinus rhythm have identifiable atrial thrombus.¹⁴ The early post-myocardial infarction period has also been recognized as a high-risk state for left atrial thrombus in patients with sinus rhythm, specifically in those with large anterior myocardial infarctions.² Thrombus formation in the cardiac chambers can be explained by Virchow's pathophysiologic principles in acute myocardial infarction.¹⁵ Enhanced thrombin activity, whether related to the acute event itself plays an essential role in thrombus formation.¹⁶ Various studies have demonstrated a rebound thrombin generation when heparin is suddenly discontinued.¹⁷ The majority of SEC and thrombus is located within LAA.^{5,18} In our study, SEC (28%) and thrombus (13%) were determined in LAA in patients with early postmyocardial infarction. Thus, in addition to the potential for left

ventricular thrombi, left ventricular dysfunction may predispose to LAA thrombus formation. Our study patients with SEC and/or thrombus had a lower left ventricular ejection fraction ($47 \pm 13\%$ vs $58 \pm 10\%$).

Color Doppler tissue imaging is a new method, which allows pulsed wave velocity measurement. Wilkenshoff et al.¹⁹ have determined that regional mean systolic velocities in the left ventricle could be evaluated through this mode and showed that their data have high reproducibility. Today regional systolic functions can be measured by recording regional average systolic myocardial velocity with real-time CDTI. We assumed that the CDTI measurements could be regionally made in the wall of LAA considering its muscular structure similar to myocardium⁷ and its strong wall movements. During its systole and diastole, LAA changes markedly in volume, which stems from active wall movements.^{7,8,20} Recently, Trambaiolo et al.²¹ have also demonstrated that the evaluation of LAA wall using transesophageal tissue Doppler is feasible, reproducible, and relatively independent from cardiac hemodynamics. In our study, SaV were measured by means of CDTI at basal, mid, and tip of LAA medial wall where the movement was observed most noticeably. Left atrial appendage dysfunction leads to stasis in cavity, which presents itself as a reduction in the LAA emptying velocity. Left atrial appendage contractile and flow velocities were reduced in patients with LAA dysfunction.²² Understandably, stasis basically develops depending on wall movement deteriorations. We demonstrated that SaV taken from the mid-SaV of medial wall of LAA were related to LAA thrombus and SEC. We have also observed that SaV decreased in patients with low LAA emptying velocity, meaning

deteriorated appendage function. This relationship suggests that CDTI could be used for the purpose of evaluating LAA function. Systolic appendage velocities taken from the basal and tip points decreased in group 1 compared to group 2, but they did not reach the value that was statistically significant. The significant decrease in SaVs obtained from the mid region may result from the difference of regional movement of the appendage wall. Another possibility may be the disorder of the regional wall movement associated with atrial infarction as in the left ventricle. Since we have not investigated atrial infarction in our patients, we are not in a position to comment on this subject.

The decline in LAA emptying velocity and LAA function^{2,20,23,24} along with other known factors,^{25–27} frequently will lead to the development of thrombus. Goldman et al.²⁸ have also reported that the low LAA emptying velocity is an important factor in the development of thrombus and thromboembolism. Assuming that the stasis developing in LAA flow will lead to thrombus and that the reason for this stasis is the decline in wall contractions, the findings we obtained can easily be explained.

STUDY LIMITATIONS

The limitations of our study are that we did not evaluate atrial infarction that may cause left atrial wall motion abnormality and the reperfusion in the group in which thrombolytic therapy was administered. Also, the number of the patients that have SEC and/or thrombus was low.

CONCLUSION

Left ventricular systolic dysfunction could precipitate blood stasis as well as thrombus formation in the LAA of patients with early postmyocardial infarction, even in the presence of sinus rhythm. Left atrial appendage emptying velocities and mid-SaVs decrease in patients with acute myocardial infarction in sinus rhythm that develop SEC and/or thrombus in LAA. Color Doppler tissue imaging appears to be a clinically applicable and reliable imaging technique that affords quantitative assessment of regional LAA systolic function.

REFERENCES

1. Black IW, Hopkins AP, Lee LC, et al. Left atrial spontaneous echo contrast: A clinical and echocardiographic analysis. *J Am Coll Cardiol* 1991;18:398–404.
2. Fatkin D, Kelly RP, Feneley MP. Relations between left atrial appendage blood flow velocity, spontaneous echocardiographic contrast, and thromboembolic risk in vivo. *J Am Coll Cardiol* 1994;23:961–969.
3. Garcia-Fernandez MA, Torrecilla EG, San Roman D, et al. Left atrial appendage Doppler flow patterns: implications on thrombus formation. *Am Heart J* 1992;124:955–961.
4. Heppell RM, Berkin KE, McLennan JM, et al. Haemostatic and haemodynamic abnormalities associated with left atrial thrombosis in non-rheumatic atrial fibrillation. *Heart* 1997;77:407–411.
5. Bilge M, Guler N, Eryonucu B, et al. Frequency of left atrial thrombus and spontaneous echocardiographic contrast in acute myocardial infarction. *Am J Cardiol* 1999;84:847–849.
6. Gorcsan J III, Gulati VK, Mandarino WA, et al. Color-coded measures of myocardial velocity throughout the cardiac cycle by tissue Doppler imaging to quantify regional left ventricular function. *Am Heart J* 1996;131:1203–1213.
7. Al-Saady NM, Obel OA, Camm AJ. Left atrial appendage: Structure, function, and role in the thromboembolism. *Heart* 1999;82:547–554.
8. Lannigan RA, Zaki SA. Ultrastructure of myocardium of the atrial appendage. *Br Heart J* 1966;28:796–807.
9. Chan SK, Kannam JP, Douglas PS, et al. Multiplane transesophageal echocardiographic assessment of left atrial appendage anatomy and function. *Am J Cardiol* 1995;76:528–530.
10. Bilge M, Eryonucu B, Guler N, et al. Transesophageal echocardiography assessment of left atrial appendage function in untreated systemic hypertensive patients in sinus rhythm. *J Am Soc Echocardiogr* 2000;13:271–276.
11. Tabata T, Oki T, Fukuda N, et al. Influence of left atrial pressure on left atrial appendage velocity patterns in patients in sinus rhythm. *J Am Soc Echocardiogr* 1996;9:857–864.
12. Oki T, Asai M, Takemura H, et al. Pulsed Doppler Echocardiographic assessment of diastolic left ventricular hemodynamics in hypertrophic cardiomyopathy: relationship between the mode of left ventricular filling and the distribution of left ventricular hypertrophy. *J Cardiol* 1983;13:523–535.
13. Ito T, Suwa M, Kobashi A, et al. Influence of altered loading conditions on left atrial appendage function in vivo. *Am J Cardiol* 1998;81:1056–1059.
14. Vigna C, Russo A, De Rito V, et al. Frequency of the left atrial thrombi by transesophageal echocardiography in idiopathic and in ischemic dilated cardiomyopathy. *Am J Cardiol* 1992;70:1500–1501.
15. Pifarre R. Thrombosis and cardiovascular disease. *Med Clin North Am* 1998;82:511–522.
16. Seitz R, Pelzer H, Immel A, et al. Prothrombin activation by thrombolytic agents. *Fibrinolysis* 1993;7:109–115.
17. Granger CB, Miller JM, Bovill EG, et al. Rebound increase in thrombin generations and activity after cessation of intravenous heparin in patients with acute coronary syndromes. *Circulation* 1995;91:1929–1935.
18. Siostrzonek P, Koppensteiner R, Gossinger H, et al. Hemodynamic and hemorheologic determinants of the left atrial spontaneous echo contrast and thrombus formation in patients with idiopathic dilated cardiomyopathy. *Am Heart J* 1993;125:430–434.
19. Wilkenshoff UM, Sovany A, Wigstrom L, et al. Regional mean systolic myocardial velocity estimation by real-time color Doppler myocardial imaging: a new technique for quantifying regional systolic function. *J Am Soc Echocardiogr* 1998;11:683–692.
20. Pollick C, Taylor D. Assessment of left atrial appendage function by transesophageal echocardiography. Implications for the development of thrombus. *Circulation* 1991;84:223–231.

21. Trambaiolo P, Salustri A, Tanga M, et al. Assessment of left atrial appendage wall velocities by transesophageal tissue Doppler echocardiography: a clinical study in patients with sinus rhythm. *J Am Soc Echocardiogr* 2002;15:425-432.
22. Hwang JJ, Li YH, Lin JM, et al. Left atrial appendage function determined by transesophageal echocardiography in patients with rheumatic mitral valve disease. *Cardiology* 1994;85:121-128.
23. Kamalesh M, Copeland TB, Sawada S. Severely reduced left atrial appendage function: a cause of embolic stroke in patients in sinus rhythm? *J Am Soc Echocardiogr* 1998;11:902-904.
24. Mugge A, Kuhn H, Nikutta P, et al. Assessment of left atrial appendage function by biplane transesophageal echocardiography in patients with nonrheumatic atrial fibrillation: identification of a subgroup of patients at increased embolic risk. *J Am Coll Cardiol* 1994;23:599-607.
25. Brickner ME, Friedman DB, Cigarroa CG, et al. Relation of thrombus in the left atrial appendage by transesophageal echocardiography to clinical risk factors for thrombus formation. *Am J Cardiol* 1994;74:391-393.
26. Igarashi Y, Yamaura M, Ito M, et al. Elevated serum lipoprotein (a) is a risk factor for left atrial thrombus in patients with chronic atrial fibrillation: a transesophageal echocardiographic study. *Am Heart J* 1998;136:965-971.
27. Peverill RE, Harper RW, Gelman J, et al. Determinants of increased regional left atrial coagulation activity in patients with mitral stenosis. *Circulation* 1996;94:331-339.
28. Goldman ME, Pearce LA, Hart RG, et al. Pathophysiologic correlates of thromboembolism in nonvalvular atrial fibrillation: I. Reduced flow velocity in the left atrial appendage (The Stroke Prevention in Atrial Fibrillation [SPAF-III] study). *J Am Soc Echocardiogr* 1999;12:1080-1087.