THROMBOLYSIS IN MYOCARDIAL INFARCTION FRAME COUNT IN SINGLE-VESSEL DISEASE AFTER ANGIOPLASTY

Chih-Hsuan Yen[1], Hung-I Yeh[1,2,3]*, Charles Jia-Yin Hou[1], Yu-San Chou[1], Cheng-Ho Tsai[1]

[1]*Section of Cardiology, Department of Internal Medicine, Mackay Memorial Hospital,*
[2]*Mackay Medicine, Nursing and Management College, and* [3]*Taipei Medical University, Taipei, Taiwan.*

SUMMARY

Background: We compared the thrombolysis in myocardial infarction (TIMI) frame count and examined the impact of angioplasty on the count between patients with normal coronary angiograms and those with single-vessel disease (SVD).
Methods: In 780 consecutive patients referred for coronary angiography, TIMI frame count was measured for 149 patients who had SVD and 32 patients with normal angiograms who underwent the procedure for electrophysiologic study or valvular heart disease survey.
Results: Comparison of each of the three vessels in the normal vessel group with the corresponding nonstenotic vessels in the SVD group showed similar counts in each of the left anterior descending artery (LAD), left circumflex artery (LCX), and right coronary artery (RCA). For the stenotic vessels, after successful angioplasty, the counts were all reduced (LAD, 54.5 ± 28.8 vs. 34.0 ± 19.3; LCX, 67.3 ± 31.1 vs. 34.1 ± 19.0; RCA, 33.2 ± 28.1 vs. 19.3 ± 7.9; all $p < 0.05$). In addition, the count in the RCA after angioplasty was lower, compared with the RCA of the normal group (19.3 ± 7.9 vs. 29.1 ± 14.6, $p = 0.001$). Multivariate analysis showed that the use of oral calcium channel blockers was the only independent predictor for the reduction in RCA after angioplasty.
Conclusion: In patients with SVD, the data of TIMI frame count in the nonstenotic vessels were similar to those without the disease, suggesting that the count in the normal artery is not affected by the adjacent stenotic artery. For the stenotic vessels, angioplasty had differential effects on each of the three arteries, indicating the existence of distinct properties, which is affected by calcium channel blockers, for individual coronary arteries in response to atherosclerosis and/or angioplasty. [International Journal of Gerontology 2007; 1(3): 125–130]

Key Words: angioplasty, coronary artery disease, TIMI frame count

Introduction

The thrombolysis in myocardial infarction (TIMI) frame count, derived by counting the number of cineangiographic frames that elapse between the contrast agent filling both sides of the proximal coronary artery and arriving at a predetermined distal landmark, is more objective and reproducible than the standard TIMI flow grade method[1]. The frame count data have been widely used in the evaluation of acute coronary syndrome and stable coronary artery disease, as well as the prediction of coronary artery restenosis and microvascular resistance[2–5]. However, such data in Taiwan are lacking. The aim of this study was to examine the value in patients with normal coronary angiograms and those with single-vessel disease (SVD), as well as to examine the impact of angioplasty on the frame count.

Materials and Methods

Patient population and study protocol

In 780 consecutive patients referred for coronary angiography from February 2003 to December 2003, normal

**Correspondence to:* Dr Hung-I Yeh, Section of Cardiology, Department of Internal Medicine, Mackay Memorial Hospital, 92 , Section 2 , Chung-San North Road, Taipei 104, Taiwan.
E-mail: hiyeh@ms1.mmh.org.tw
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coronary angiograms and TIMI frame count were obtained in 32 patients who underwent the procedure for the purpose of electrophysiologic study or valvular heart disease survey, without any significant coronary artery stenosis. Coronary angiograms and TIMI frame count were also measured in 149 patients with SVD, i.e., presence of over 50% luminal stenosis in only one of the three major coronary arteries. Excluded from the consecutive series were patients with prior coronary bypass surgery, acute myocardial infarction within the preceding 24 hours, or previous cardiac transplantation. In those with SVD, 74 patients (50%) had lesions with more than 70% stenosis and underwent angioplasty. TIMI frame counts were measured in each of the three coronary arteries of both the normal and SVD group, including the target vessel after angioplasty.

TIMI frame count evaluation

A TIMI frame count was determined for each major coronary artery in each patient according to the methods first described by Gibson et al.[1]. Briefly, the number of coronary angiogram frames, recorded with 30 frames per second required for the leading edge of the column of radiographic contrast to reach a predetermined landmark, was determined[5]. The first frame is defined as the frame in which fully concentrated dye occupies the full width of the proximal artery lumen, touching both borders of the lumen and proceeds down the artery in a forward motion. The final frame is determined when the leading edge of the contrast column initially arrives at the distal landmark. In the left anterior descending artery (LAD), the landmark used is the most distal branch nearest the apex of the left ventricle, commonly referred to as the "pitchfork" or "whale's tail"[1]. The right coronary artery (RCA) distal landmark is the first branch of the posterior-lateral RCA after the origin of the posterior descending artery, regardless of the size of this branch. If a significant stenosis is present within the posterior descending artery, the landmark is the first branch of the posterior descending artery itself beyond the stenosis. However, the distal landmark in the left circumflex artery (LCX) system was defined as the most distal branch of the artery containing the infarct-related stenosis originally. Because the current study was performed in non-infarct condition, the branch of the circumflex or marginal artery that composed the greatest total distance traveled by contrast was used to define the distal landmark if there was no significant stenosis. Finally, the TIMI frame count in the LAD and LCX were evaluated in a right anterior oblique projection with caudal angle view and the RCA in a left anterior oblique projection with cranial angle view.

Variables and definitions

Patient and clinical variables for analysis included age, gender, body mass index (BMI, kg/m^2), hypertension (defined as systolic blood pressure ≥ 140 mmHg and/or diastolic blood pressure ≥ 90 mmHg diastolic blood pressure on repeated measurements, or permanent antihypertensive drug treatment), diabetes mellitus (defined as a fasting blood glucose concentration ≥ 126 mg/dL, or antihyperglycemic drug treatment), hyperlipidemia (serum total cholesterol > 240 mg/dL or serum triglyceride > 160 mg/dL), current smoking (defined as having smoked the last cigarette less than 1 week before coronary angiography), and long-term medication use before the study (defined as separate variables for the use of any aspirin, ticlopidine/clopidogrel, nitrate, angiotensin-converting enzyme inhibitors, angiotensin II receptor antagonist, calcium channel blocker, statin, and diuretics). Hemodynamic variables were left ventricular ejection fraction (by echocardiography or left ventriculography), systolic pressure and diastolic blood pressure, and left ventricular end-diastolic pressure.

Statistical analysis

TIMI frame counts (expressed as mean ± standard deviation) were compared for each artery, between those with and without stenosis according to the variables. Univariate analysis of all continuous variables with TIMI frame count was performed using unpaired *t* tests, primarily to determine which variables should be entered into the multivariate analysis model. A *p* value of less than 0.05 was required for significance of variables in the model. All independent dichotomous variables were performed using chi-square method. Multivariate analysis was performed with SPSS software version 11.0.

Results

Baseline characteristics of all patients are presented in Table 1. There were no significant differences in age, blood pressure, ejection fraction and left ventricular end-diastolic pressure between the normal group and the SVD group. The baseline characteristics for patients with SVD are in Table 2. There were no significant clinical

Table 1.	*Baseline characteristics of all patients*	
	Normal CAG ($n=32$)	SVD ($n=149$)
Age (yr)	59.8±13.5	63.1±12.9
Gender (female)*, *n* (%)	15 (46.8)	55 (36.9)
BMI*	24.6±3.9	26.1±4.6
Hypertension*, *n* (%)	13 (40.6)	114 (76.5)
Diabetes mellitus*, *n* (%)	4 (12.5)	43 (28.8)
Hyperlipidemia*, *n* (%)	2 (6.2)	41 (27.5)
Current smoker*, *n* (%)	9 (28.1)	59 (39.5)
Systolic blood pressure (mmHg)	143.9±30.6	142.6±28.8
Diastolic blood pressure (mmHg)	75.2±11.8	72.4±13.8
LVEDP (mmHg)	19.4±7.9	17.9±6.9
Ejection fraction (%)	64.3±10.7	63.2±10.3

**p*<0.05 between the groups. CAG = coronary angiogram; SVD = single-vessel disease; BMI = body mass index; LVEDP = left ventricular end-diastolic pressure.*

differences among the three coronary arteries, except with the use of diuretics.

Regarding TIMI frame counts, comparison of each of the three vessels in the normal group and the corresponding nonstenotic vessels in the SVD group showed no significant difference in the LAD, LCX, and RCA, respectively (Table 3). In addition, the data of each artery in the normal and diseased groups were not affected by gender, except the group with diseased LAD and RCA (Table 4).

Data of TIMI frame count after angioplasty in each of the three vessels are shown in Table 5. Compared with the normal group, the frame count in RCA after successful angioplasty was lower (19.3±7.9 vs. 29.1±14.6, $p=0.001$). A similar trend existed for LAD (34.0±19.3 vs. 39.4±16.0, $p=0.18$) but not for LCX (34.1±19.1 vs. 33.3±11.8, $p=0.46$), compared with the normal vessel.

Univariate analyses showed that the significant variable affecting the frame count of RCA after angioplasty

Table 2.	*Baseline characteristics of patients with single-vessel disease (SVD) according to the location of lesion*		
	LAD ($n=94$)	LCX ($n=18$)	RCA ($n=37$)
Age	63.8±12.3	59.3±13.4	59.0±14.2
Gender (female), *n* (%)	36 (38.2)	7 (38.8)	12 (32.4)
BMI	24.9±4.8	27.0±4.0	27.3±4.5
Hypertension, *n* (%)	73 (77.6)	13 (72.2)	28 (75.6)
Diabetes mellitus, *n* (%)	30 (31.9)	5 (27.7)	8 (21.6)
Hyperlipidemia, *n* (%)	23 (24.4)	7 (38.8)	11 (29.7)
Current smoker, *n* (%)	33 (35.1)	10 (55.5)	16 (43.2)
Systolic blood pressure (mmHg)	146.1±30.3	135.9±24.2	136.9±24.9
Diastolic blood pressure (mmHg)	72.7±14.9	75.4±10.1	70.3±12.0
LVEDP (mmHg)	17.3±6.9	18.9±5.9	18.9±7.3
Ejection fraction (%)	62.3±10.1	57.8±11.8	66.0±10.3
Medicine use, *n* (%)			
Aspirin	48 (51.0)	11 (61.1)	22 (59.4)
Ticlopidine/Clopidogrel	47 (50.0)	9 (50)	23 (62.1)
Nitrate	51 (54.2)	11 (61.1)	20 (54.0)
ACE inhibitor	45 (47.8)	10 (55.5)	12 (32.4)
ARB	20 (21.2)	3 (16.6)	13 (35.1)
Calcium channel blocker	33 (35.1)	6 (33.3)	10 (27.0)
Beta-blocker	37 (39.3)	13 (72)	14 (37.8)
Statin	21 (22.3)	8 (44)	14 (37.8)
Diuretic*	21 (22.3)	2 (11)	4 (10.8)

**p* < 0.05 between the groups. LAD=left anterior descending artery; LCX=left circumflex artery; RCA=right coronary artery; BMI=body mass index; LVEDP=left ventricular end-diastolic pressure; ACE=angiotensin-converting enzyme; ARB=angiotensin II receptor antagonist.*

Table 3. *Thrombolysis in myocardial infarction (TIMI) frame count of normal coronary artery in patients with all three normal arteries (designated as no coronary artery disease [CAD]) and those with single-vessel disease (SVD)*

	TIMI frame count	p*
LAD		0.25
No CAD ($n=31$)	39.4 ± 16.0	
SVD ($n=55$)	42.2 ± 19.3	
Total ($n=86$)	41.2 ± 18.1	
LCX		0.2
No CAD ($n=31$)	33.3 ± 11.8	
SVD ($n=131$)	36.2 ± 18.1	
Total ($n=162$)	35.7 ± 17.1	
RCA		0.18
No CAD ($n=29$)	29.1 ± 14.6	
SVD ($n=112$)	26.5 ± 13.2	
Total ($n=141$)	27.0 ± 13.4	

**Derived from comparison between the patients with no CAD and those with the corresponding SVD. LAD = left anterior descending artery; LCX = left circumflex artery; RCA = right coronary artery.*

Table 4. *TIMI frame count of normal coronary artery in the group with no coronary artery disease (CAD) and those groups with single-vessel disease*

		TIMI frame count	p*
LAD			
No CAD	Male ($n=16$)	38.5 ± 13.3	0.38
	Female ($n=15$)	40.3 ± 18.8	
CAD	Male ($n=36$)	47.3 ± 11.9	0.0004
	Female ($n=19$)	31.9 ± 7.2	
LCX			
No CAD	Male ($n=35$)	33.6 ± 10.4	0.43
	Female ($n=19$)	32.9 ± 13.5	
CAD	Male ($n=48$)	37.1 ± 19.3	0.199
	Female ($n=83$)	34.5 ± 15.8	
RCA			
No CAD	Male ($n=15$)	29.2 ± 10.9	0.48
	Female ($n=14$)	29.0 ± 17.4	
CAD	Male ($n=69$)	28.7 ± 14.2	0.004*
	Female ($n=43$)	22.7 ± 10.3	

**Derived from comparison between the genders of the same group. LAD = left anterior descending artery; LCX = left circumflex artery; RCA = right coronary artery.*

Table 5. *Thrombolysis in myocardial infarction (TIMI) frame count of vessels after angioplasty and vessels of the group with no coronary artery disease (CAD)*

Target vessel of angioplasty	TIMI frame count before angioplasty	TIMI frame count after angioplasty	No CAD	TIMI frame count	p*
LAD ($n=45$)	54.5 ± 28.8	34.0 ± 19.3	LAD ($n=31$)	39.4 ± 16.0	0.18
LCX ($n=7$)	67.3 ± 31.1	34.1 ± 19.0	LCX ($n=31$)	33.3 ± 11.8	0.46
RCA ($n=22$)	33.2 ± 28.1	19.3 ± 7.9	RCA ($n=29$)	29.1 ± 14.6	0.001

**Derived from comparison between the target vessel after angioplasty and the corresponding normal vessel. LAD = left anterior descending artery; LCX = left circumflex artery; RCA = right coronary artery.*

was the use of oral calcium channel blocker ($p=0.01$; Table 6).

Multivariate analyses showed that the use of calcium channel blocker was still associated with a significantly lower TIMI frame counts ($p=0.02$; Table 6) in RCA after angioplasty, compared with those of the corresponding normal coronary artery.

Discussion

This study showed that, for normal coronary artery, the data of TIMI frame count in patients with all three normal coronary arteries and in those with SVD were similar. The finding is consistent with a study conducted in people from the West[5]. After angioplasty, the count number was markedly reduced in all three stenotic vessels. However, only the number in RCA after angioplasty was significantly lower than that of the RCA in patients with all three normal coronary arteries. Although we do not know the exact mechanism underlying such a drastic reduction in RCA, one possibility may be due to the existence of poststenotic dilatation of the diseased vessel before angioplasty. After relief of the stenosis, the flow downstream of the dilated lesion may increase and reach a level higher

Table 6. *Results of univariate analysis for right coronary artery vessel (n = 22) with angioplasty*

Clinical variable	*p*
Sex	0.24
Hypertension	0.22
Hyperlipidemia	0.37
Current smoker	0.41
Diabetes	0.37
Prior MI	0.34
CHF history	0.15
Medicine use	
Aspirin	0.31
Beta-blocker	0.20
Calcium channel blocker	0.01*
ACE inhibitor	0.29
ARB	0.47
Statin	0.42
Nitrate	0.45
Hemodynamic factor	
EF > 50%	0.26
LVEDP > 18 mmHg	0.13

**$p < 0.05$ between the with and without groups. MI = myocardial infarction; CHF = congestive heart failure; ACE = angiotensin-converting enzyme; ARB = angiotensin II receptor antagonist; EF = ejection fraction; LVEDP = left ventricular end-diastolic pressure.*

than a normal artery, and therefore, the frame count is lower than the normal artery. In addition, routine intracoronary use of nitrate during angioplasty is also expected to shorter the count number, as shown in a previous study[6]. However, in comparison with RCA, the post-angioplasty count numbers in the LAD and LCX were not significantly lower when compared with the corresponding normal arteries; this may be attributed to the ventricular pressure, which is lower in the right side, from where the RCA is harvested, than the left side, where the LAD and LCX are located.

In the present study, univariate analyses showed that the use of oral calcium channel blockers had lower frame counts in RCA after angioplasty. The result was also confirmed by multivariate analyses. Intracoronary injection of calcium channel blockers had proved to be effective in preventing distal embolism, and this may shorten the TIMI frame count after angioplasty in acute myocardial infarction[7,8]. The calcium T-channel blocker mibefradil was also reported to effectively reduce anginal symptom in coronary slow flow phenomenon[9]. However, the effect of intracoronary delivery of calcium channel blockers may not be the same as that of the oral forms, which has not been evaluated before. Nevertheless, in the present study, we found an extraordinary impact of oral calcium channel blockers on RCA frame count after angioplasty.

Despite the presence of numerous potential factors that may introduce variability into the TIMI frame count method, only body size, systemic arterial pressure, age, and sex are reportedly significant factors[5]. In the present study, we did observe differences in the frame count for LAD and RCA between genders in patients with SVD. Some previous studies revealed that the variation of the frame count remained narrow, but other data did not support the finding[1,5]. In the present study, the variation of the frame count was wider, because lesions of chronic total occlusion were included and the frame count number was given as 99.

Previous reports suggested that measurement of TIMI frame counts is a simple and reliable method to estimate coronary flow reserve[10], but not all studies agreed on this point[11–13]. In addition, some investigators claimed that TIMI frame count divided by minimal luminal diameter can be used to predict coronary artery restenosis after angioplasty[14]. Although there is still controversy about the clinical use of the frame count, it is really a simple and available method for collection of the data.

In conclusion, the data of TIMI frame count in the nonstenotic vessels were similar to those without coronary artery disease. For the stenotic vessels, angioplasty had differential effects on each of the three arteries. These findings suggest that distinct properties exist for individual coronary arteries in response to atherosclerosis and/or angioplasty. Routine use of oral calcium channel blockers before angiography accelerates the coronary blood flow after angioplasty in the RCA, implying that the response to the interventional procedure is vessel-specific.

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References

1. Gibson CM, Cannon CP, Daley WL, Dodge JT, Alexander B, Marble SJ, et al. TIMI frame count: a quantitative method of assessing coronary artery flow. Circulation 1996; 93: 879–88.
2. Gibson CM, Murphy SA, Rizzo MJ, Ryan KA, Marble SJ, McCabe CH, et al. Relationship between TIMI frame count and clinical outcomes after thrombolytic administration. Circulation 1999; 99: 1945–50.
3. Gibson CM, Cannon CP, Greene RM, Sequeira RF, Margorien RD, Leya F, et al. Rescue angioplasty in the thrombolysis in myocardial infarction (TIMI) 4 trial. Am J Cardiol 1997; 80: 21–6.
4. Gibson CM, Rizzo M, McLean C, Dotani I, Goel M, Ryan K, et al. The TIMI frame count and restenosis: faster is better. J Am Coll Cardiol 1997; 29: 201A.
5. Faile BA, Guzzo JA, Tate DA, Nichols TC, Smith SC, Dehmer GJ. Effect of sex, hemodynamics, body size, and other clinical variables on the corrected thrombolysis in myocardial infarction frame count used as an assessment of coronary blood flow. Am Heart J 2000; 140: 308–14.
6. Abaci A, Oguzhan A, Eryol NK, Ergin A. Effect of potential confounding factors on the thrombolysis in myocardial infarction (TIMI) trial frame count and its reproducibility. Circulation 1999; 100: 2219–23.
7. Hang CL, Wang CP, Yip HK, Yang CH, Guo BF, Wu CJ, et al. Early administration of intracoronary verapamil improves myocardial perfusion during percutaneous coronary interventions for acute myocardial infarction. Chest 2005; 128: 2593–8.
8. Gerald SW, Klaus L, Helmuth K, Hans RF. Intracoronary verapamil for reversal of no-reflow during coronary angioplasty for acute myocardial infarction. Catheter Cardiovasc Interv 2002; 57: 444–51.
9. Beltrame JF, Turner SP, Leslie SL, Solomon P, Freedman SB, Horowitz JD. The angiographic and clinical benefits of mibefradil in the coronary slow flow phenomenon. J Am Coll Cardiol 2004; 44: 57–62.
10. Manginas A, Gatzov P, Chasikidis C, Voudris V, Pavlides G, Cokkinos DV. Estimation of coronary flow reserve using the Thrombolysis In Myocardial Infarction (TIMI) frame count method. Am J Cardiol 1999; 83: 1562–5.
11. Tanedo JS, Kelly RF, Marquez M, Burns DE, Klein LW, Costanzo MR, et al. Assessing coronary blood flow dynamics with the TIMI frame count method: comparison with simultaneous intracoronary Doppler and ultrasound. Catheter Cardiovasc Interv 2001; 53: 459–63.
12. Ohara Y, Hiasa Y, Takahashi T, Yamaguchi K, Ogura R, Ogata T, et al. Relation between the TIMI frame count and the degree of microvascular injury after primary coronary angioplasty in patients with acute anterior myocardial infarction. Heart 2005; 91: 64–7.
13. Chugh SK, Koppel J, Scott M, Shewchuk L, Goodhart D, Bonan R, et al. Coronary flow velocity reserve does not correlate with TIMI frame count in patients undergoing non-emergency percutaneous coronary intervention. J Am Coll Cardiol 2004; 44: 778–82.
14. Stankovic G, Manginas A, Voudris V, Pavlides G, Athanassopoulos G, Ostojic M, et al. Prediction of restenosis after coronary angioplasty by use of a new index: TIMI frame count/minimal luminal diameter ratio. Circulation 2000; 101: 962–8.