

심근기절이 원격 관상동맥 혈류예비력에 미치는 영향

가

문건웅 · 김재형 · 유기동 · 윤호중 · 정옥성 · 채장성 · 최규보 · 홍순조

Effects of Myocardial Stunning on Remote Coronary Flow Reserve

Keon Woong Moon, MD, Jae Hyung Kim, MD, Ki Dong Yoo, MD, Ho Joong Youn, MD,
Wook Sung Chung, MD, Jang Seong Chae, MD, Kyu Bo Choi, MD and Soon Jo Hong, MD

Department of Internal Medicine, Catholic University Medical College, Seoul, Korea

ABSTRACT

Background : In patients with myocardial infarction (MI) and chronic stable angina, the coronary flow reserve (CFR) is reduced not only in the region of myocardium perfused by the ischemia-related artery but also in the regions supplied by angiographically normal coronary arteries. The effect of myocardial stunning on the remote CFR is unknown, however. **Methods** : In ten open-chest anesthetized dogs, left circumflex coronary artery was occluded for 15 minutes (myocardial stunning group, n=5) or for 30 minutes (MI group, n=5) and was followed by a reperfusion for 60 minutes. Before coronary occlusion and at 30 minutes and at 60 minutes after reperfusion, resting coronary blood flow (CBF) and maximal CBF after injection of each of adenosine (ADE) and acetylcholine (Ach) was measured with electromagnetic flow probe located in the proximal left anterior descending coronary artery. CFR was calculated as the ratio of maximal and resting CBF. **Results** : At 30 minutes and 60 minutes after reperfusion, the remote resting CBF were significantly increased in both groups and the remote CFR was significantly decreased in both groups. The CFR of the MI group was lower than myocardial stunning group. The coronary vasodilator response to Ach was significantly lower than the response to ADE in both groups. **Conclusion** : After MI and myocardial stunning, there was severe coronary vasodilator abnormality in the remote myocardium and that was more marked after MI. The coronary vasodilator response to Ach was significantly lower than the response to ADE in both groups, suggesting endothelial dysfunction in remote myocardium. (Korean Circulation J 1998;28(12):2002-2010)

KEY WORDS : Coronary flow reserve · Myocardial infarction · Myocardial stunning · Remote myocardium.

서 론

가

1)2)

3)

4)

(myocardial stunning)

: 1998 9 17

: 1999 2 5

: , 150 - 010

62

가

: (02) 3779 - 1114 · : (02) 3779 - 1374

5)

E - mail : echo1@cmc.cuk.ac.kr

amine HCL,)
 (Ventilator, animal 683,
 Havard, USA) 35 40 , 1
 15 20 ml/kg
 50 75 mg(2.5% 2 3 ml)
 (Thiopental sodium 0.5 g, Sodium carbonate 0.03
 g,) 가
 5
 10)11) 가 2 3cm
 가 (electromagnetic blood flow probe)
 12) (Cliniflow , Model FM 701D, Carolina Medical EI -
 가 electronic inc, North Carolina, USA)
 가
 가 (snare)
 (Fig. 1).
 5F pigtail catheter

재료 및 방법

혈역학적 변화의 측정

실험 동물

10 15.6 ± 1.8 kg(14 18 kg)
 . 1 2 mg/kg (Ket -

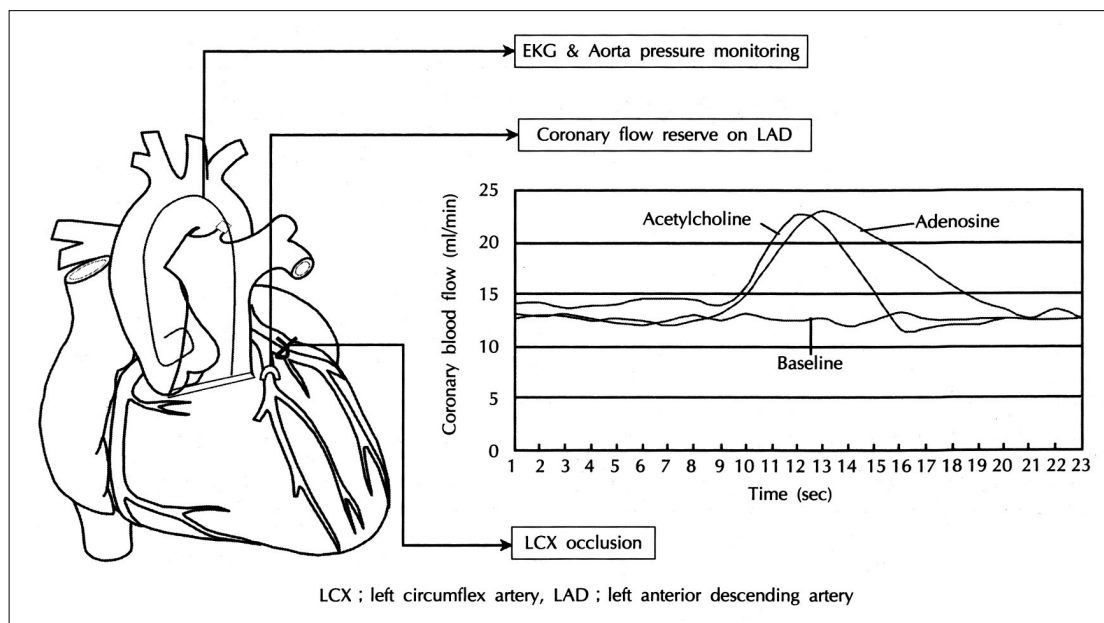


Fig. 1. Experimental procedure of left circumflex artery occlusion.

Adenosine(9-β-D-ribofuranosyladenine)(Sanofi Winthrobe Ltd) 1.5 μg/kg

Acetylcholine 0.01 μg/kg

(mmHg · min/ml) = (mmHg) (ml/min)

SPSS for MS Windows Release 6.0
Wilcoxon Rank Sum

W Test
Wilcoxon Signed - Ranks Test

(Fig. 2)

10 (n=5)

p<0.05

결 과

30 60
enosine acetylcholine

기저상태의 혈역학적 변화
adenosine acetylcholine

30 60
enosine acetylcholine

가
osine acetylcholine
가 . Aden -

관상동맥 혈류예비력 및 관상동맥 저항 측정

(ml/min)

adenosine 90 ± 5.9 mmHg
(p<0.05) 108 ± 5.2 mmHg

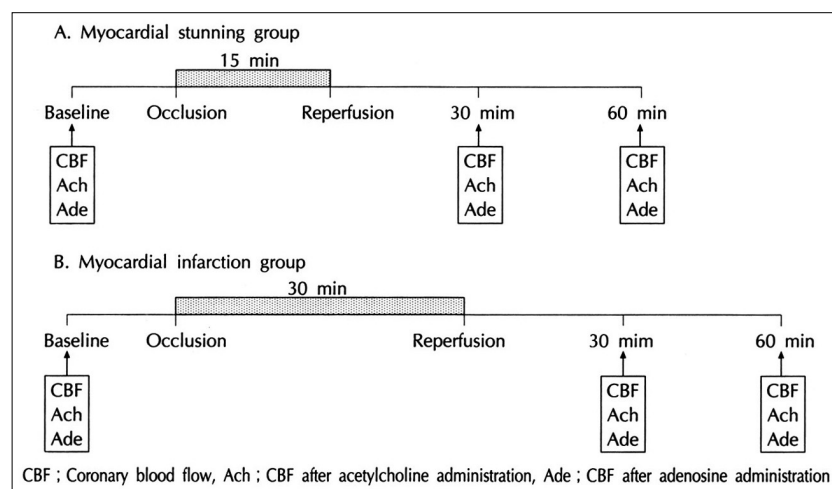


Fig. 2. Experimental protocol.

adenosine 91 ± 5.7 mmHg
(p<0.05). acetylcholine 91 ± 4.7 mmHg (p<0.05), 93 ± 6.7 mmHg (p<0.05) adenosine acetylcholine 가 (Table 1).

관상동맥 폐쇄 후 재관류시 혈역학적 변화

30 (mmHg) 99 ± 9.2
111 ± 4.6 (p<0.05),
(mmHg · min/ml) 6.4 ±
0.76 7.7 ± 0.42 (p<0.01).

Adenosine acetylcholine 가 (ml/
min) (21.
2 ± 0.75 vs 19.3 ± 1.17, p<0.05)(Table 3).

Adenosine 가
, 82 ± 4.4 mm Hg, 심근기절군에서 원격심근 관상동맥 혈류예비력의 변화
75 ± 4.9 mmHg (p<0.05) adenosine
가 . acetylcholine 가 30

Table 1. Baseline hemodynamic data

	Resting	Adenosine	Ach
Heart rate (bpm)			
Stunning group	99 ± 3.6	99 ± 3.8	98 ± 3.8
MI group	100 ± 9.7	95 ± 6.2	94 ± 5.3
MAP (mmHg)			
Stunning group	104 ± 4.0	90 ± 5.9*	91 ± 4.7*
MI group	108 ± 5.2	91 ± 5.7*	93 ± 6.7*
CBF (ml/min)			
Stunning group	12.2 ± 0.70	23.1 ± 1.41*	22.5 ± 1.68*
MI Group	12.6 ± 0.55	23.3 ± 1.55*	22.8 ± 2.27*
CVR (mmHg · min/ml)			
Stunning group	8.5 ± 0.27	3.9 ± 0.21*	4.1 ± 0.36*
MI group	8.6 ± 0.76	3.9 ± 0.51*	4.1 ± 0.58*

* : p<0.05 vs baseline

MAP : mean arterial pressure (mmHg)

CBF : coronary blood flow (ml/min)

CVR : coronary vascular resistance (mmHg · min/ml)

Resting : hemodynamic values at resting state

Adenosine : hemodynamic values after adenosine administration

Ach : hemodynamic values after acetylcholine administration

Table 2. Hemodynamic data at reperfusion 30 min

	Resting	Adenosine	Ach
Heart rate (bpm)			
Stunning group	98 ± 6.2	94 ± 3.7	97 ± 4.5
MI group	103 ± 6.9	97 ± 5.7	103 ± 5.1
MAP (mmHg)			
Stunning group	105 ± 6.1	82 ± 4.4	84 ± 4.0
MI group	98 ± 5.6	75 ± 4.9*	82 ± 6.9
CBF (ml/min)			
Stunning group	15.5 ± 0.47	25.6 ± 1.11	22.2 ± 0.86
MI Group	16.3 ± 0.88	24.8 ± 1.53	19.5 ± 0.67 [†]
CVR (mmHg · min/ml)			
Stunning group	6.7 ± 0.52	3.2 ± 0.23	3.8 ± 0.26
MI group	6.0 ± 0.60	3.0 ± 0.29	4.2 ± 0.35

* : p<0.05 vs stunning group

[†] : p<0.01 vs stunning group

MAP : mean arterial pressure (mmHg)

CBF : coronary blood flow (ml/min)

CVR : coronary vascular resistance (mmHg · min/ml)

Resting : hemodynamic values at resting state

Adenosine : hemodynamic values after adenosine administration

Ach : hemodynamic values after acetylcholine administration

Table 3. Hemodynamic data at reperfusion 60 min

	Resting	Adenosine	Ach
Heart rate (bpm)			
Stunning group	95 ± 6.9	95 ± 4.8	93 ± 5.2
MI group	102 ± 6.4	96 ± 5.8	100 ± 5.6
MAP (mmHg)			
Stunning group	111 ± 4.6	82 ± 7.5	80 ± 7.6
MI group	99 ± 9.2*	80 ± 4.0	80 ± 6.8
CBF (ml/min)			
Stunning group	14.5 ± 0.62	24.3 ± 1.50	21.2 ± 0.75
MI Group	15.6 ± 0.96	23.3 ± 1.43	19.3 ± 1.17*
CVR (mmHg · min/ml)			
Stunning group	7.7 ± 0.42	3.4 ± 0.35	3.8 ± 0.32
MI group	6.4 ± 0.76†	3.4 ± 0.35	4.1 ± 0.24

* : p<0.05 vs stunning group

† : p<0.01 vs stunning group

MAP : mean arterial pressure (mmHg)

CBF : coronary blood flow (ml/min)

CVR : coronary vascular resistance (mmHg · min/ml)

Resting : hemodynamic values at resting state

Adenosine : hemodynamic values after adenosine administration

Ach : hemodynamic values after acetylcholine administration

60 adenosine (1.9 ± 0.05,
30 1.7 ± 0.09, 60 1.7 ± 0.12)
acetylcholine (1.8 ± 0.11, 30
1.4 ± 0.07, 60 1.5 ± 0.09)
(p<0.05). acetylcholine
adenosine
(30 ; 1.4 ± 0.07 vs 1.7 ± 0.09, p<0.05,
60 ; 1.5 ± 0.09 vs 1.7 ± 0.12, p<0.05) (Figs.
3 and 5).

심근경색군에서 원격심근 관상동맥 혈류예비력의 변화

adenosine
acetylcholine 가 30
60 adenosine (1.9 ± 0.08,
30 1.5 ± 0.06, 60 1.5 ± 0.14) acety -
lcholine (1.8 ± 0.19, 30 1.2
± 0.04, 60 1.2 ± 0.01) (p<0.
05). acetylcholine
adenosine (30 ; 1.2 ± 0.04 vs 1.5 ± 0.06, p<0.05, 60
; 1.2 ± 0.01 vs 1.5 ± 0.14, p<0.05) (Fig. 4).

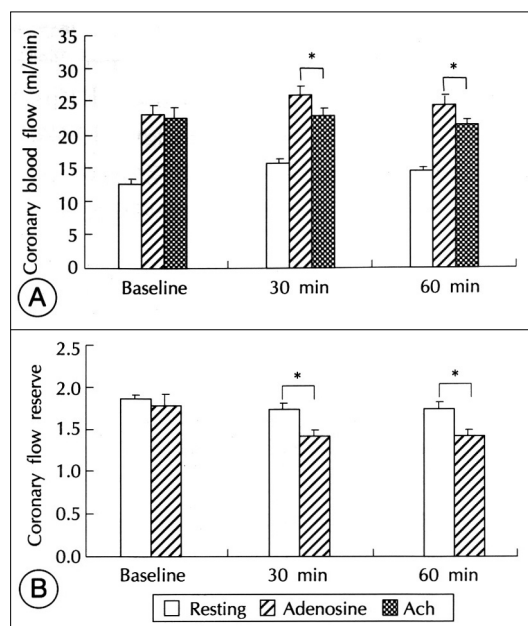


Fig. 3. Bar graphs of the effects of myocardial stunning on the remote myocardium. **Panel A** : Resting and hyperemic coronary blood flows at baseline and at 30 min & 60 min after reperfusion. At baseline, hyperemic coronary blood flows after adenosine and after acetylcholine were similar, whereas after reperfusion the responses to acetylcholine were significantly lower than the responses to adenosine. **Panel B** : Effects of myocardial stunning on the remote coronary flow reserve (CFR). At baseline, there was no significant difference between the CFR after adenosine and the CFR after acetylcholine, whereas the CFR after adenosine were significantly lower than the CFR after acetylcholine (* : p<0.05).

심근기절군과 심근경색군의 원격 관상동맥혈류예비력의 비교

acetylcholine
가
30 60
(30 p<0.01,
60 p<0.01), adenosine
가 30
(p<0.05)
60
(p=0.0917)
(Table 4, Fig. 5).
acetylcholine
adenosine
(30 p<0.05, 60 p<0.05).

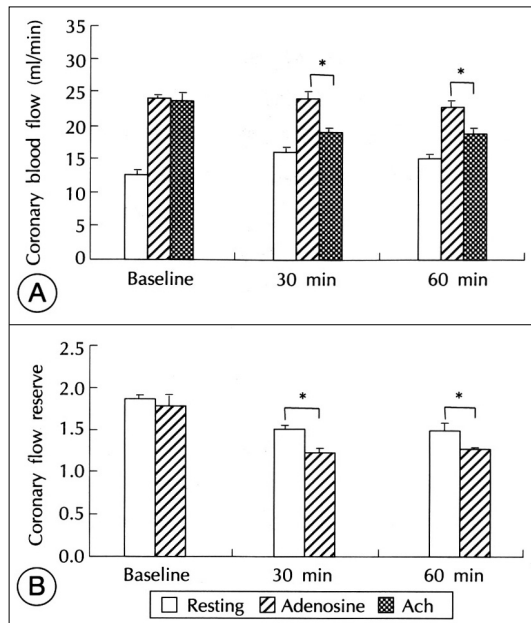


Fig. 4. Bar graphs of the effects of myocardial infarction on the remote myocardium. **Panel A :** Resting and hyperemic coronary blood flows at baseline and at 30 min & 60 min after reperfusion. At baseline, hyperemic coronary blood flows after adenosine and acetylcholine were similar, whereas after reperfusion the responses to acetylcholine were significantly lower than the responses to adenosine. **Panel B :** Effects of myocardial infarction on the remote coronary flow reserve (CFR). At baseline, there was no significant difference between the CFR after adenosine and the CFR after acetylcholine, whereas the CFR after adenosine were significantly lower than the CFR after acetylcholine (* : $p < 0.05$).

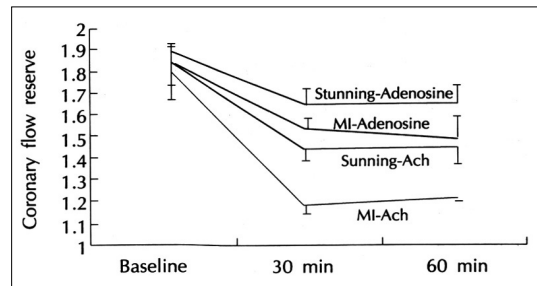


Fig. 5. Effects of myocardial stunning and myocardial infarction (MI) on the remote coronary flow reserve (CFR). At baseline, both groups show similar CFR. After coronary artery occlusion and reperfusion, the CFR of both stunning and MI group decreased. The CFR of MI group was significantly lower than the CFR of myocardial stunning group in response to acetylcholine (Ach) at reperfusion 30 min and 60 min ($p < 0.05$, $p < 0.05$ respectively) and in response to adenosine at reperfusion 30 min ($p < 0.05$). The CFR after Ach administration decreased further than the CFR after adenosine infusion in both groups ($p < 0.01$ in both groups).

Table 4. Coronary flow reserve in both groups

	Baseline	30 min	60 min
Myocardial stunning group			
Adenosine	1.89 ± 0.05	$1.65 \pm 0.09^*$	$1.69 \pm 0.12^*$
Ach	1.84 ± 0.11	$1.43 \pm 0.07^{*\dagger}$	$1.47 \pm 0.09^{*\dagger}$
Myocardial infarction group			
Adenosine	1.85 ± 0.08	$1.52 \pm 0.06^*$	$1.50 \pm 0.14^*$
Ach	1.81 ± 0.19	$1.19 \pm 0.04^{*\dagger}$	$1.24 \pm 0.01^{*\dagger}$

Adenosine : hemodynamic values after adenosine administration
Ach : hemodynamic values after acetylcholine administration

* : $p < 0.05$ vs baseline

† : $p < 0.05$ vs adenosine

고찰

Heyndrickx¹⁾

5

3, 15, 6

가

ker,¹³⁾ Bolli¹⁴⁾ 20

Kloner AI-

Braunwald²⁾

(myocardial stunning)

15)

16)

(sarcoplasmic reticulum)

(excitation-contraction uncoupling),¹⁷⁾

18)

19)

3 4

(low reflow phenomenon)

(coronary flow)

Korean Circulation J 1998;28(12):2002-2010

가
acetylcholine
30 60 , adenosine
30
acetylcholine
adenosine
가

연구배경 :

결 론 :

acetylcholine
adenosine
가

중심 단어 :

가

1998

REFERENCES

- 방 법 :
10
adenosine(1.5 μ g/kg)
acetylcholine(0.01 μ g/kg)
(ml/min) (n = 5)
15
(n = 5) 30
30 60
adenosine acetylcholine
- 결 과 :
가
가 30 60
가 30
60
30 60
- Heyndrickx GR, Millard RW, McRitchie RJ. *Regional myocardial functional and electrophysiological alterations after brief coronary occlusion in conscious dog.* J Clin Invest 1975;56:978-85.
 - Braunwald E, Kloner RA. *The stunned myocardium: Prolonged, postischemic ventricular dysfunction.* Circulation 1982;66:1146-9.
 - Braunwald E. *The stunned myocardium: Newer insights into mechanism and clinical implications.* J Thorac Cardiovasc Surg 1990;100:310-1.
 - Fournier C, Boujon B, Hebert J. *Stunned myocardium following coronary spasm.* Am Heart J 1991;121:593-5.
 - Coffman JD, Gregg DE. *Reactive hyperemic characteristics of the myocardium.* Am J Physiol 1960;199:1143-9.
 - Youn HJ, Chung WS, Kim JJ, Park JC, Kim CM, Chae JS, et al. *Evaluation of coronary flow reserve by transesophageal doppler echocardiography in patients with chest pain and normal coronary angiogram.* Korean Circulation J 1996; 26:431-41.
 - Pichard AD, Gorlin R, Smith H, Ambrose J, Meller J. *Coronary flow studies in patients with left ventricular hypertrophy of the hypertensive type - Evidence for an impaired coronary vascular reserve.* Am J Cardiol 1981;47: 547-54.
 - Opherk D, Zebe H, Weihe E, Mall G, Durr C, Gravert B, et al. *Reduced coronary dilatory capacity and ultrastructural changes of the myocardium in patients with angina pectoris but normal coronary arteriograms.* Circulation 1981;63:817-25.
 - Opherk D, Mall G, Zebe H, Schwarz F, Weihe E, Mant-

- hey J, et al. Reduction of coronary reserve: A mechanism for angina pectoris in patients with arterial hypertension and normal coronary arteries. *Circulation* 1984;69:1-7.
- 10) Uren NG, Marraccini P, Gistri R, de Silva R, Camici Pg. Altered coronary vasodilator reserve and metabolism in myocardium subtended by normal arteries in patients with coronary artery disease. *J Am Coll Cardiol* 1993;22:650-8.
- 11) Sambuceti G, Parodi O, Marcassa C, Neglia D, Salvadori P, Giorgetti A, et al. Alteration in regulation of myocardial blood flow in one-vessel coronary artery disease determined by positron emission tomography. *Am J Cardiol* 1993;72:538-43.
- 12) Uren NG, Crake T, Lefroy DC, de Silva R, Davies GJ, Marseri A. Reduced coronary vasodilator function in infarcted and normal myocardium after myocardial infarction. *N Engl J Med* 1994;331:222-7.
- 13) Kloner RA, Alker KJ. The effect of streptokinase on the intram-yocardial hemorrhage, infarct size, and the no-reflow phenomenon during coronary reperfusion. *Circulation* 1984;70:513-21.
- 14) Bolli R, Triana JF, Jeroudi Mo. Prolonged impairment of coronary vasodilation after reversible ischemia. Evidence for microvascular stunning. *Circ Res* 1990;67:332-43.
- 15) Park CG, Kim YH, Park HN, Lee SC, Yim DS, Han SW, et al. Effect of L-arginine on post-ischemic myocardial and vascular stunning in the open-chest dogs. *Korean Circulation J* 1996;26:88-99.
- 16) Tani M, Neely JR. Role of intravascular Na^+ in Ca^{2+} overload and depressed recovery of ventricular function of reperfused ischemic hearts: Possible involvement of H^+ - Na^+ and Na^+ - Ca^{2+} exchange. *Circ Res* 1989;65:1045-56.
- 17) Krause SM, Jacobus WE, Becker LC. Alteration in cardiac sarcoplasmic reticulum calcium transport in the post-ischemic "stunned" myocardium. *Circ Res* 1989;65:526-30.
- 18) Przyklenk K, Kloner RA. Superoxide dismutase plus catalase improve contractile function in the canine model of the "stunned" myocardium. *Circ Res* 1986;58:148-56.
- 19) Zhao M, Zhang H, Robinson TF, Factor SM, Sonnenblick EH, Eng C. Profound structural alteration of the extracellular collagen matrix in postischemic dysfunctional but viable myocardium. *J Am Coll Cardiol* 1987;10:1322-34.
- 20) Heyndrickx GR, Baig H, Nellens P, Leusen I, Fishbein MC, Vatner SF. Depression of regional blood flow and wall thickening after brief coronary occlusion. *Am J Physiol* 1978;234:H653-H9.
- 21) Kim YH. The effect of reperfusion after brief, reversible myocardial ischemia on coronary vascular function and ultrastructure. *Korean Circulation J* 1996;26:405-19.
- 22) Jeremy RW, Stahl L, Gillinov M, Litt M, Aversano TR, Becker LC. Preservation of coronary flow reserve in stunned myocardium. *Am J Physiol* 1989;256:H1303-H10.
- 23) Stahl LD, Aversano TR, Secker LC. Selective enhancement of function of stunned myocardium by increased flow. *Circulation* 1987;74:843-51.
- 24) Rechavia E, de Silva R, Nihoyannopoulos P, Lammertsma AA, Jones T, Maseri A. Hyperdynamic performance of remote myocardium in acute infarction. Correlation between regional contractile function and myocardial perfusion. *E Heart J* 1995;16:1845-50.
- 25) Kramer M, Rogers WJ, Theobald TM, Power TP, Petruolo S, Reichel N. Remote noninfarcted region dysfunction soon after first anterior myocardial infarction. A magnetic resonance tagging study. *Circulation* 1996;94:660-6.
- 26) Beyersdorf F, Acar C, Buckberg GD, Partington MT, Sjöstrand F, Young HH, et al. Studies on prolonged acute regional ischemia. Early natural history of simulated single and multivessel disease with emphasis on remote myocardium. *J Thorac Cardiovasc Surg* 1989;98:368-80.
- 27) Marsch SCU, Wanigasekera VA, Ryder WA, Wong LSS, Foex P. Graded myocardial ischemia is associated with a decrease in diastolic distensibility of the remote nonischemic myocardium in the anesthetized dog. *J Am Coll Cardiol* 1993;22:899-906.