

## 급성 관동맥 증후군의 위험도 판정

박 성 훈

### Risk Stratification of Acute Coronary Syndrome

Seong-Hoon Park, MD

Department of Internal Medicine, College of Medicine, Ewha Womans University, Seoul, Korea

#### ABSTRACT

The "ACC/AHA Guideline Update for the management of patients with unstable angina and Non-ST-segment elevation myocardial infarction", which was published in 2002, emphasizes the continuous risk stratification of patients with unstable angina and non-ST-elevation myocardial infarction (NSTEMI), during the course of its diagnosis and management. The main purpose of the risk stratification in patients with acute coronary syndrome is to identify high risk patients, and give them optimal treatment, in an optimal environment, and to prevent inappropriate, or excessive, treatment for patients with a low risk of an adverse outcome. For patients with an intermediate risk at the initial evaluation, further risk stratification, with noninvasive diagnostic tests, is recommended, which may provide a guide for the next treatment plan. For the initial risk stratification of patients with suspected acute coronary syndrome; the clinical history, a physical examination, a 12-lead electrocardiography and cardiac specific biomarkers, are critically important. Cardiac specific troponins, T and I, are especially useful for the diagnosis of acute coronary syndrome, and they may also provide important information for the risk stratification. There are two main strategies for the management of acute coronary syndrome; the early invasive and the early conservative, strategies. There are many reports suggesting the positive effect of the early invasive strategy, compared with the early conservative strategy, on the prognosis of high risk patients. Low molecular weight heparin and GP-IIb/IIIa receptor blockers have been reported to provide a positive effect on the prognosis when used in high risk patients. Therefore, the risk stratification is important during the diagnostic procedure, and may provide an important guide in the management of patients with acute coronary syndrome. (**Korean Circulation J 2002;32(9):739-755**)

**KEY WORDS** : Angina, unstable ; Myocardial infarction ; Risk ; Troponin.

#### 서 론

2002 "ACC/AHA Guideline Update for the management of patients with unstable angina and Non - ST - segment elevation myocardial infarc-

tion " (unstable angina) NS-TEMI(non - ST - elevation myocardial infarction)

.<sup>1)</sup> 가

, 가

: , 158 - 710 911 - 1

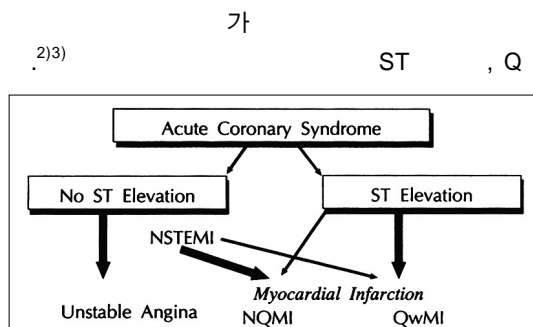
: (02) 650 - 5018 · : (02) 650 - 5424

E - mail : psh7935@chollian.net

가

(early invasive strategy)  
 (early conservative strategy)  
 가 , 가  
 가  
 GP - b/ a re-  
 ceptor blocker 가

### 급성관동맥증후군



**Fig. 1.** Nomenclature of ACSs. Patients with ischemic discomfort may present with or without ST-segment elevation on the ECG. The majority of patients with ST-segment elevation (large arrows) ultimately develop a Q-wave AMI (QwMI), whereas a minority (small arrow) develop a non-Q-wave AMI (NQMI). Patients who present without ST-segment elevation are experiencing either UA or an NSTEMI. The distinction between these 2 diagnoses is ultimately made based on the presence or absence of a cardiac marker detected in the blood. Most patients with NSTEMI do not evolve a Q wave on the 12-lead ECG and are subsequently referred to as having sustained a non-Q-wave MI (NQMI); only a minority of NSTEMI patients develop a Q wave and are later diagnosed as having Q-wave MI. Not shown is Prinzmetal's angina, which presents with transient chest pain and ST-segment elevation but rarely MI. The spectrum of clinical conditions that range from UA to non-Q-wave AMI and Q-wave AMI is referred to as ACSs. Reproduced with permission. ACC/AHA guidelines for the management of patients with unstable angina and non-ST segment elevation myocardial infarction : a report of the ACC/AHA Task Force on Practice Guidelines. JACC 2000 ; 36 : 970-1062.

Q  
 , Q  
 (Fig. 1). National Heart Attack Alert Program(NHAAP)

가  
 가 , 12  
 10  
 4) NSTEMI 가  
 가  
 가 ,  
 가 1) a) ST -  
 (STEMI)  
 , b) NSTEMI, c) , 2)  
 ( ; ,  
 , ) 3)  
 ( ; , ),  
 4)

### 초기 평가와 치료

가 ,  
 가?  
 가?  
 가

ACC/AHA Class

“	가 20
	,
	.
	.”

**Table 1.** Likelihood that signs and symptoms represent an ACS secondary to CAD

Feature	High likelihood Any of the following :	Intermediate likelihood Absence of high-likelihood features and presence of any of the following :	Low likelihood Absence of high- or intermediate-likelihood features but may have :
History	Chest or left arm pain or discomfort as chief symptom reproducing prior documented angina Known history of CAD, including MI	Chest or left arm pain or discomfort as chief symptom Age >70 years Male sex Diabetes mellitus	Probable ischemic symptoms in absence of any of the intermediate likelihood characteristics Recent cocaine use
Examination	Transient MR, hypotension, diaphoresis, pulmonary edema, or rales	Extracardiac vascular disease	Chest discomfort reproduced by palpation
ECG	New, or presumably new, transient ST-segment deviation ( $\geq 0.05$ mV) or T-wave inversion ( $\geq 0.2$ mV) with symptoms	Fixed Q waves Abnormal ST segments or T waves not documented to be new	T-wave flattening or inversion in leads with dominant R waves Normal ECG
Cardiac markers	Elevated cardiac Tnl, TnT, or CK-MB	Normal	Normal

Reproduced with permission. ACC/AHA guidelines for the management of patients with unstable angina and non-ST segment elevation myocardial infarction : a report of the ACC/AHA Task Force on Practice Guidelines. JACC 2000 ; 36 : 970-1062. ACS : acute coronary syndrome, CAD : coronary artery disease

**Table 2.** Short-Term risk of death or nonfatal MI in patients With UA\*

Feature	High Risk At least 1 of the following features must be present :	Intermediate risk No high-risk feature but must have 1 of the following :	Low risk No high- or intermediate-risk feature but may have any of the following features :
History	Accelerating tempo of ischemic symptoms in preceding 48 h	Prior MI, peripheral or cerebrovascular disease, or CABG, prior aspirin use	
Character of pain	Prolonged ongoing (>20 minutes) rest pain	Prolonged (>20 min) rest angina, now resolved, with moderate or high likelihood of CAD Rest angina (<20 min) or relieved with rest or sublingual NTG	New-onset or progressive CCS Class III or IV angina the past 2 weeks without prolonged (>20 min) rest pain but with moderate or high likelihood of CAD (see Table 5)
Clinical findings	Pulmonary edema, most likely due to ischemia New or worsening MR murmur S <sub>3</sub> or new/worsening rales Hypotension, bradycardia, tachycardia Age >75 years	Age >70 years	
ECG	Angina at rest with transient ST-segment changes >0.05 mV Bundle-branch block, new or presumed new Sustained ventricular tachycardia	T-wave inversions >0.2 mV Pathological Q waves	Normal or unchanged ECG during an episode of chest discomfort
Cardiac markers	Elevated (e.g., TnT or Tnl >0.1 ng/mL)	Slightly elevated (e.g., TnT<0.01 but <0.1 ng/mL)	Normal

Reproduced with permission. ACC/AHA guidelines for the management of patients with unstable angina and non-ST segment elevation myocardial infarction : a report of the ACC/AHA Task Force on Practice Guidelines. JACC 2000 ; 36 : 970-1062.

\* : estimation of the short-term risks of death and nonfatal cardiac ischemic events in UA is a complex multivariable problem that cannot be fully specified in a table such as this ; therefore, this table is meant to offer general guidance and illustration rather than rigid algorithms

가  
 , 2  
 . 1) 가  
 가  
 가(Table 1)? 2) 가 가  
 가(Table 2)? , , , . 가 1) ( ,  
 , , , ) 2) GP b/ a  
 가 .

### 초기 위험도 평가

가 ACC/AHA  
 .  
 Class  
 1)  
 가 ,  
 ,  
 2)  
 , ,  
 .  
 3)  
 (10 ) 12-  
 ,  
 가 가  
 .  
 4)  
 . troponin  
 , 가  
 . CK - MB  
 6 가  
 6~12  
 ( , 9 )  
 .  
 \* : ACC/AHA class  
 가 가  
 가

### 위험도평가의 이론적 배경

가  
 가 . 가  
 가  
 2  
 4-7)  
 PURSUIT,<sup>5)</sup> ESSENCE<sup>8)</sup>  
 NSTEMI 24,774  
 .  
 65 ,  
 , CCS  
 ,  
 ST . PURSUIT  
 .  
 NSTEMI  
 병 력

협심증 증상  
 “ ACC/AHA/ACP - ASIM  
 guidelines for the management of patients with ch-  
 ronic stable angina. <sup>19)</sup>  
 가 가

(5) , 18)19)

) . 가  
가

,  
.  
, , ,  
. ,  
가

내원시 초기 위험도의 예측  
NSTEMI

(angina equivalents) . 가 . Beorsma 20)  
30  
.  
, , ST - ,  
,  
가 . Antman 21) 7 ( 65 ,  
3 ,  
, ST - , 24 2  
, 7  
) .  
,  
가  
10) ST (STEMI) , 가  
TIMI 5% 41%  
가 TIMI TIMI - 11B 22)  
, NSTEMI 가 ESSENCE, 23) TACTICS - TIMI - 18 24)  
11)12) 가 PRISM - PLUS 7) 가 .  
NSTEMI 가 가  
13)14) 22)23)  
70 가 GP b/ a 25) 24)  
가 가  
( , ,  
) 가  
15)16)  
, 따라서 이들 전  
통적 위험인자들의 유무에 의해 환자를 급성관동맥증후  
군으로 입원시키거나 치료할 것인지를 결정해서는 안된  
다. ( , )  
17) STEMI NSTEMI 5)  
가 , 20  
3 , ,

1 mm ST - T

27)

진찰소견

6%

30

30

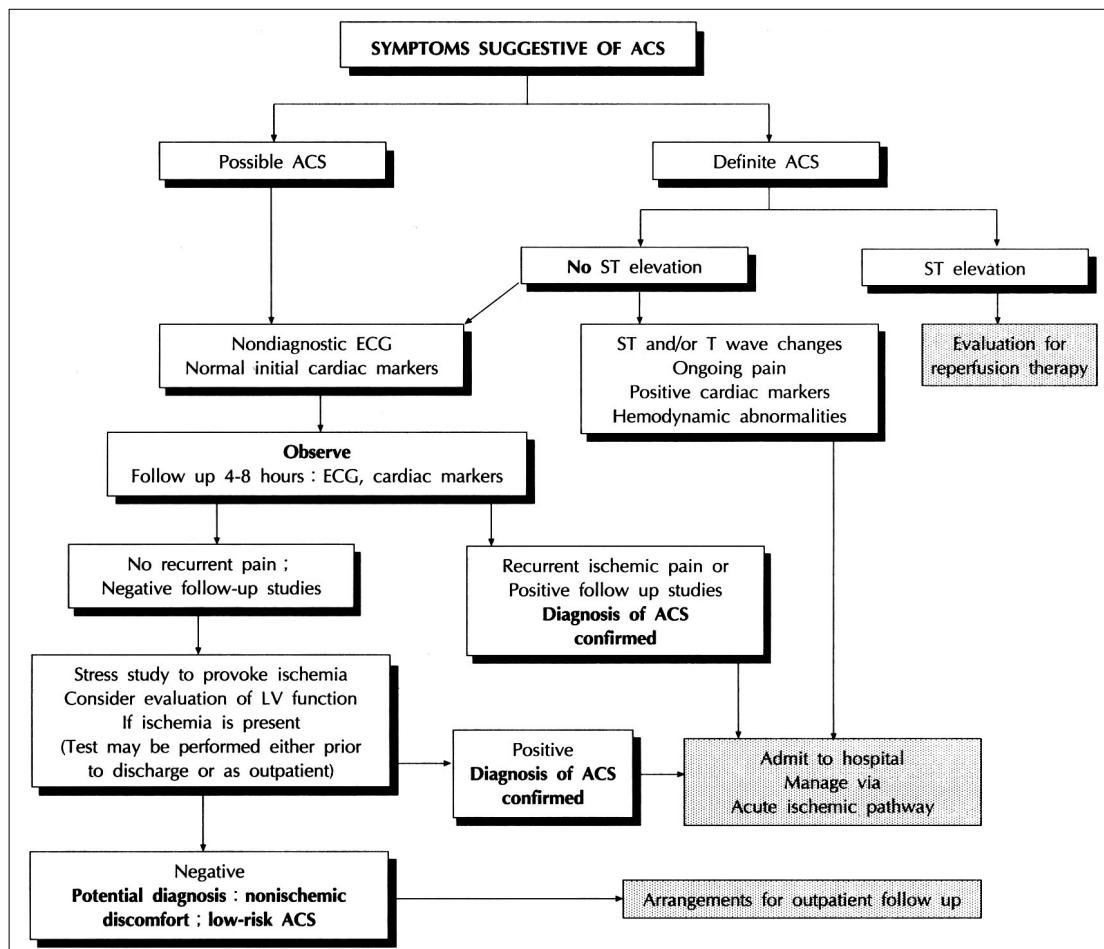
가

1.2%,

1.7%

vital sign

( , , )



**Fig. 2.** Algorithm for evaluation and management of patients suspected of having ACS. Reproduced with permission. ACC/AHA guidelines for the management of patients with unstable angina and non-ST segment elevation myocardial infarction : a report of the ACC/AHA Task Force on Practice Guidelines. JACC 2000 ; 36 : 970-1062. ACS : acute coronary syndrome, LV : left ventricle

bruit pulse deficit  
가

NSTEMI

SHOCK,<sup>28)</sup> GUSTO - ,<sup>29)</sup> PURSUIT<sup>5)</sup>

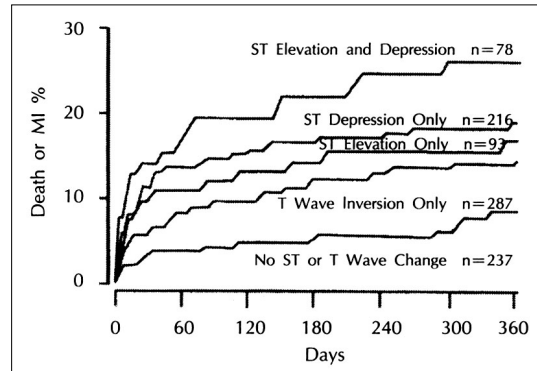
NSTEMI 5%

60%

### 위험도 판정을 위한 도구들

심전도

가  
가 가<sup>30-32)</sup>  
가  
가 ST - (0.05 mV )  
가  
가  
가 가 가<sup>33)34)</sup>  
12  
가  
가  
(Fig. 2). NSTEMI CK -  
MB가 25% Q  
75% Q ST -  
ST - V1 V3  
ST -  
T -<sup>35)</sup>  
Q  
(0.2 mV ) T -  
<sup>36)</sup> 1~6%가



**Fig. 3.** Adverse outcome by initial ECG in ACS. Reproduced with permission. ACC/AHA guidelines for the management of patients with unstable angina and non-ST segment elevation myocardial infarction : a report of the ACC/AHA Task Force on Practice Guidelines. JACC 2000 ; 36 : 970-1062. ACS : acute coronary syndrome.

NSTEMI

4%

가  
가  
<sup>31)37)</sup>  
ST - T -  
ST -  
Prinzmetal's  
Wolf - Parkinson - White  
tricyclic antidepressant  
phenothiazine  
T -  
(Fig. 3).<sup>38)39)</sup>  
가  
ST - ( )  
가 T -  
가 가  
<sup>38-41)</sup>  
12  
<sup>30)</sup>  
ST -

생화학적 심근 표지자 들

CK - MB

CK - MB isoform(subform)

CK - MB2 CK - MB1

CK - MB2/CK - MB1

CK - MB

CK - MB

Cardiac troponins

Troponin TnT, TnI, TnC

TnI

TnT(cTnT)

TnI(cTnI)

TnC isoform

TnC

cTnT cTnI가

cTnT cTnI

CK - MB가

troponin

CK - MB

troponin

troponin

ST -

CK - MB가

30%

NSTEMI

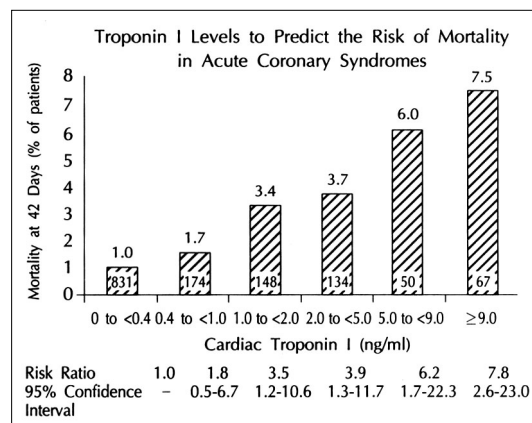
cTnI

cTnT cTnI

(Fig. 4).

ST -

troponin



**Fig. 4.** Relationship between cardiac troponin levels and risk of mortality in patients with ACS. Reproduced with permission. ACC/AHA guidelines for the management of patients with unstable angina and non-ST segment elevation myocardial infarction : a report of the ACC/AHA Task Force on Practice Guidelines. JACC 2000 ; 36 : 970-1062. ACS : acute coronary syndrome.



**Table 3.** Biochemical cardiac markers for the evaluation and management of patients with suspected ACS but without ST-T segment elevation on 12-lead ECG

Marker	Advantages	Disadvantages	Point of care test available?	Comment	Clinical recommendation
CK-MB	Rapid, cost-efficient, accurate assays Ability to detect early reinfarction	Loss of specificity in setting of skeletal muscle disease or injury, including surgery Low sensitivity during very early MI (6 h after symptom onset) or later after symptom onset (>36 h) and for minor myocardial damage (detectable with troponins)	Yes	Familiar to majority of clinicians	Prior standard and still acceptable diagnostic test in most clinical circumstances
CK-MB isoforms	Early detection of MI	Specificity profile similar to that of CK-MB Current assays require special expertise	No	Experience to date predominantly in dedicated research centers	Useful for extremely early (3 - 6 h after symptom onset) detection of MI in centers with demonstrated familiarity with assay technique
Myoglobin	High sensitivity Useful in early detection of MI Detection of reperfusion Most useful in ruling out MI	Very low specificity in setting of skeletal muscle injury or disease Rapid return to normal range limits sensitivity for later presentations	Yes	More convenient early marker than CK-MB isoforms because of greater availability of assays for myoglobin Rapid-release kinetics make myoglobin useful for noninvasive monitoring of reperfusion in patients with established MI	
Cardiac troponins	Powerful tool for risk stratification Greater sensitivity and specificity than CKMB Detection of recent MI up to 2 weeks after onset Useful for selection of therapy Detection of reperfusion	Low sensitivity in very early phase of MI (<6 h after symptom onset) and requires repeat measurement at 8 - 12 h, if negative Limited ability to detect late minor reinfarction	Yes	Data on diagnostic performance and potential therapeutic implications increasingly available from clinical trials	Useful as a single test to efficiently diagnose NSTEMI (including minor myocardial damage), with serial measurements. clinicians should familiarize themselves with diagnostic "cutoffs" used in their local hospital laboratory

Reproduced with permission. ACC/AHA guidelines for the management of patients with unstable angina and non-ST segment elevation myocardial infarction : a report of the ACC/AHA Task Force on Practice Guidelines. JACC 2000 ; 36 : 970-1062. ACS : acute coronary syndrome

GP b/ a

CAPTURE troponin

23.9%, abcix - imab  
9.5% (p=0.002),<sup>60)</sup> troponin

7.5%, abciximab 9.4%  
(p=NS). 가 GP b/ a tirofiban<sup>61)</sup>  
cTnT, cTnI dalteparin<sup>62)</sup>

FRISC

Myoglobin  
Myoglobin  
heme

CK - MB troponin

2

myoglobin

24

가 가

4~8  
myoglobin

cTnT, cTnI CK - MB  
<sup>63)64)</sup> myoglobin  
4~8

가

12 가

ST - 가

3 . Troponin “

가

troponin

troponin

CK - MB

Troponin

CK - MB

Myoglobin

NSTEMI

troponin

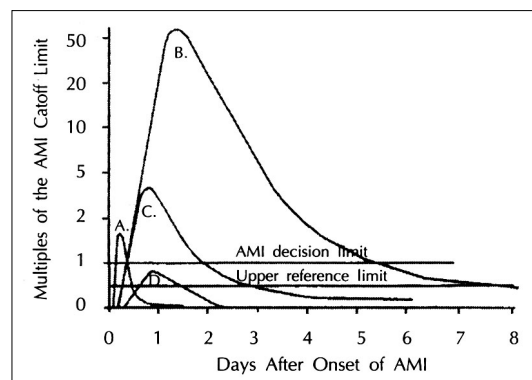
troponin

6

6

8~12

tropo-



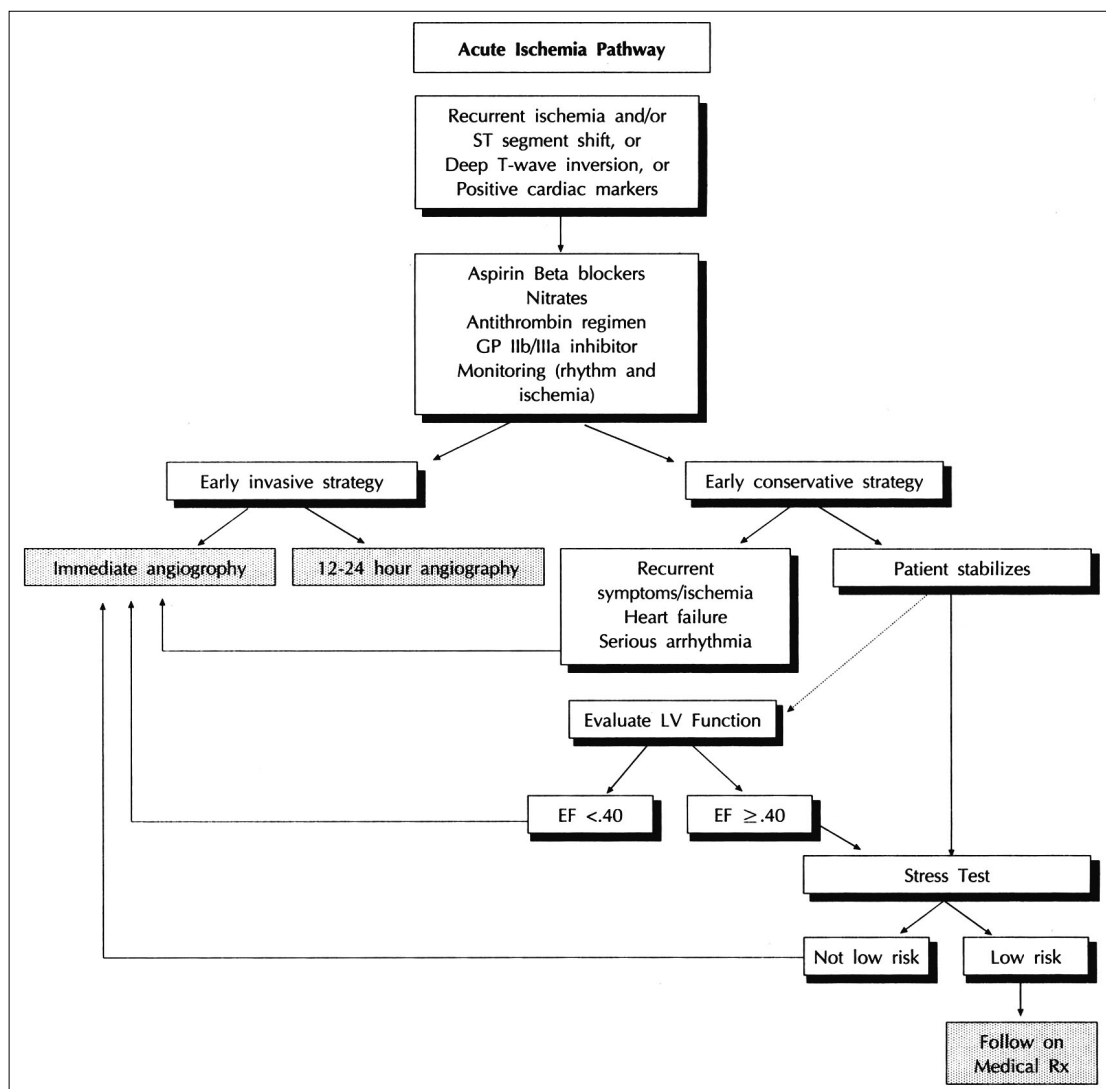
**Fig. 5.** Plot of the appearance of cardiac markers in blood vs. time after onset of symptoms. Peak A, early release of myoglobin or CK-MB isoforms after AMI. Peak B, cardiac troponin after AMI. Peak C, CK-MB after AMI. Peak D, cardiac troponin after UA. Data are plotted on a relative scale, where 1.0 is set at the AMI cutoff concentration. Reproduced with permission. ACC/AHA guidelines for the management of patients with unstable angina and non-ST segment elevation myocardial infarction : a report of the ACC/AHA Task Force on Practice Guidelines. JACC 2000 ; 36 : 970-1062.

Table

가

(Fig. 5).<sup>49)65 - 67)</sup>

troponin (10~14 )  
 , troponin  
 myoglobin  
 CRP, serum amyloid A,<sup>70)</sup> interleukin - 6  
 brinopeptide,<sup>68)</sup> fibrinogen<sup>69)</sup>



**Fig. 6.** Acute ischemia pathway. Reproduced with permission. ACC/AHA guidelines for the management of patients with unstable angina and non-ST segment elevation myocardial infarction : a report of the ACC/AHA Task Force on Practice Guidelines. JACC 2000 ; 36 : 970-1062.

CRP가  
71-74) BNP

natriuretic peptide

75)

## 비관혈적검사들을 이용한 위험도판정

(Fig. 2, 6) 가  
ACC/AHA .

Class		
1)	(Table 2) 가	12~24
2)	(Table 2) 가	2~3
3)	가 가 ST - 가 가 WPW digoxin 가	
4)	ST - (0.1 mV ), 가 가 WPW digoxin 가	
5)	( , , , 가 가	
6)	가	
Class	a	

(	가
)	
* : ACC/AHA class	
가	가
가	가
. ACC/AHA class	
가	
가	
. a	가

**Table 4.** Noninvasive risk stratification

### High risk (>3% annual mortality rate)

1. Severe resting LV dysfunction (LVEF <0.35)
2. High-risk treadmill score (score - 11)
3. Severe exercise LV dysfunction(exercise LVEF <0.35)
4. Stress-induced large perfusion defect (particularly if anterior)
5. Stress-induced multiple perfusion defects of moderate size
6. Large, fixed perfusion defect with LV dilatation or increased lung uptake (thallium-201)
7. Stress-induced moderate perfusion defect with LV dilatation or increased lung uptake (thallium-201)
8. Echocardiographic wall motion abnormality (involving >2 segments) developing at a low dose of dobutamine (10 mg/kg/min) or at a low heart rate (<120 bpm)
9. Stress echocardiographic evidence of extensive ischemia

### Intermediate risk (1 - 3% annual mortality rate)

1. Mild/moderate resting LV dysfunction (LVEF 0.35 - 0.49)
2. Intermediate-risk treadmill score ( - 11 < score <5)
3. Stress-induced moderate perfusion defect without LV dilatation or increased lung intake (thallium-201)
4. Limited stress echocardiographic ischemia with a wall motion abnormality only at higher doses of dobutamine involving 2 segments

### Low risk (<1% annual mortality rate)

1. Low-risk treadmill score (score 5)
2. Normal or small myocardial perfusion defect at rest or with stress
3. Normal stress echocardiographic wall motion or no change of limited resting wall motion abnormalities during stress

Reproduced with permission. ACC/AHA guidelines for the management of patients with unstable angina and non-ST segment elevation myocardial infarction : a report of the ACC/AHA Task Force on Practice Guidelines. JACC 2000 ; 36 : 970-1062.

**Table 5.** Noninvasive test results that predict high risk for adverse outcome (LV imaging)

Stress radionuclide ventriculography		Stress echocardiography	
Exercise EF	0.50	Rest EF	0.35
Rest EF	0.35	Wall motion score index > 1	
Fall in EF	0.10		

Reproduced with permission. ACC/AHA guidelines for the management of patients with unstable angina and non-ST segment elevation myocardial infarction : a report of the ACC/AHA Task Force on Practice Guide-lines. JACC 2000 ; 36 : 970-1062.

2)

ACC/AHA Guidelines for Exercise Testing, ACC/AHA Guidelines for the Clinical Use of Cardiac Radionuclide Imaging ACC/AHA Guidelines for the Clinical Application of Echocardiography

(Table 4, 5).<sup>76-78)</sup>

#### 6.5 Mets

, treadmill score가 (- 11 )

가

<sup>79)</sup>

가

가

가

(6.5

METS , treadmill score 5 )<sup>79)</sup>

가

. 6.5 METS

(0.2 mV

ST

(

,

),

(

0.35

)

ST

6

ST

가

)가

가

가

VANQWISH

Q

442

Thallium spect

<sup>82)</sup>

가

238

1, 6, 12

3%, 10%, 13%

1%, 3%, 6%

#### 관동맥조영술의 선택

가

가

ACC/

AHA Guidelines for Coronary Angiography

<sup>83)</sup>

중심 단어 : ; ; ;

## REFERENCES

- Braunwald E, Antman EM, Beasley JW, Califf RM, Cheitlin MD, Hochman JS, Jones RH, Kereiakes D, Kupersmith J, Levin TN, Pepine CJ, Schaeffer JW, Smith EE 3rd, Steward DE, Theroux P. ACC/AHA guideline update for the management of patients with unstable angina and non-ST-segment elevation myocardial infarction. *Am J Cardiol* 2002 update. Available from: [http://www. acc.org/ clinical/guidelines/unstable/incorporated/index.htm](http://www.acc.org/clinical/guidelines/unstable/incorporated/index.htm). Accessed March 30, 2002.
- Braunwald E. Unstable angina: an etiologic approach to management. *Circulation* 1998;98:2219-22.
- Braunwald E. Unstable angina: a classification. *Circulation* 1989;80:410-4.
- Anderson HV, Cannon CP, Stone PH, Williams DO, McCabe CH, Knatterud GL, Thompson B, Willerson JT, Braunwald E. One-year results of the thrombolysis in myocardial infarction (TIMI) IIIB clinical trial: a randomized comparison of tissue-type plasminogen activator versus placebo and early invasive versus early conservative strategy in unstable angina and non-Q wave myocardial infarction. *J Am Coll Cardiol* 1995;26:1643-50.
- PURSUIT Trial investigators. Inhibition of platelet glycoprotein IIb/IIIa with eptifibatide in patients with acute coronary syndromes: platelet glycoprotein IIb/IIIa in unstable angina: receptor suppression using integrin therapy. *N Engl J Med* 1998;339:436-43.
- TIMI Trial Investigators. Effects of tissue plasminogen activator and a comparison of early invasive and conservative strategies in unstable angina and non-Q-wave myocardial infarction: thrombolysis in myocardial ischemia. *Circulation* 1994;89:1545-56.
- Platelet Receptor Inhibition in Ischemic Syndrome Management in Patients Limited by Unstable Signs and Symptoms (PRISM-PLUS) Study Investigators. Inhibition of the platelet glycoprotein IIb/IIIa receptor with tirofiban in unstable angina and non-Q-wave myocardial. *N Engl J Med* 1998;338:1488-97.
- Cohen M, Stinnett SS, Weatherly B, Gurfinkel ED, Frommell GJ, Goodman SG, Fox KA, Califf RM. Predictors of recurrent ischemic events and death in unstable coronary artery disease after treatment with combination antithrombotic therapy. *Am Heart J* 2000;139:962-70.
- Gibbons RJ, Chatterjee K, Daley J, Douglas JS, Fihn SD, Gardin JM, Grunwald MA, Levy D, Lytle BW, O'Rourke RA, Schafer WP, Williams SV, Ritchie JL, Cheitlin MD, Eagle KA, Gardner TJ, Garson A Jr, Russell RO, Ryan TJ, Smith SC Jr. ACC/AHA/ACP-ASIM guidelines for the management of patients with chronic stable angina. *J Am Coll Cardiol* 1999;33:2092-197.
- Briege DB, Mak KH, White HD, Kleiman NS, Miller DP, Vahanian A, Ross AM, Califf RM, Topol EJ. Benefit of early sustained reperfusion in patients with prior myocardial infarction (the GUSTO-I trial): global utilization of streptokinase and TPA for occluded arteries. *Am J Cardiol* 1998;81:282-7.
- Hochman JS, McCabe CH, Stone PH, Becker RC, Cannon CP, DeFeo-Fraulini T, Thompson B, Steingart R, Knatterud G, Braunwald E. Outcome and profile of women and men presenting with acute coronary syndromes: a report from TIME IIIB. *J Am Coll Cardiol* 1997;30:141-8.
- Scirica BM, Moliterno DJ, Every NR, Anderson HV, Aguirre FV, Granger CB, Lambrew CT, Rabbani LE, Arnold A, Sapp SK, Booth JE, Ferguson JJ, Cannon CP. Differences between men and women in the management of unstable angina pectoris (the GUARANTEE Registry). *Am J Cardiol* 1999;84:1145-50.
- Holmes DJ Jr, White HD, Pieper F, Ellis SG, Califf RM, Topol EJ. Effect of age on outcome with primary angioplasty versus thrombolysis. *J Am Coll Cardiol* 1999;33:412-9.
- White HD, Barbash GI, Califf RM, Simes RJ, Granger CB, Weaver WD, Kleiman NS, Aylward PE, Gore JM, Vahanian A, Lee KL, Ross AM, Topol EJ. Age and outcome with contemporary thrombolytic therapy: global utilization of streptokinase and TPA for occluded coronary arteries trial. *Circulation* 1996;94:1826-33.
- Selker HP, Griffith JL, D'Agostino RB. A tool for judging coronary care unit admission appropriateness, valid for both real-time and retrospective use: a time-insensitive predictive instrument (TIPI) for acute cardiac ischemia multicenter study. *Med Care* 1991;29:610-27.
- Jayes RL Jr, Beshansky JR, D'Agostino RB, Selker HP. Do patients' coronary risk factor reports predict acute cardiac ischemia in the emergency department?: a multi-center study. *J Clin Epidemiol* 1992;45:621-6.
- Mak KH, Moliterno DJ, Granger CB, Miller DP, White HD, Wilcox RG, Califf RM, Topol EJ. Influence of diabetes mellitus on clinical outcome in the thrombolytic era of acute myocardial infarction. *J Am Coll Cardiol* 1997;30:171-9.
- Mueller HS, Cohen LS, Braunwald E, Forman S, Feit F, Ross A, Schweiger M, Cabin H, Davison R, Miller D. Predictors of early morbidity and mortality after thrombolytic therapy of acute myocardial infarction: analyses of patient subgroups in the thrombolysis in myocardial infarction (TIMI) trial, phase II. *Circulation* 1992;85:1254-64.
- Barbash GI, White HD, Modan M, Diaz R, Hampton JR, Heikkila J, Kristinsson A, Mouloupoulos S, Paolasso EA, van der Werf T. Significance of smoking in patients receiving thrombolytic therapy for acute myocardial infarction. *Circulation* 1993;87:53-8.
- Beersma E, Pieper KS, Steyerberg EW, Wilcox RG, Chang WC, Lee KL, Akkerhuis KM, Harrington RA, Deckers JW, Armstrong PW, Lincoff AM, Califf RM, Topol EJ, Simoons ML. Predictors of outcome in patients with acute coronary syndromes without persistent ST-segment elevation: results from an international trial of 9461 patients. *Circulation* 2000;101:2557-67.
- Antman EM, Cohen M, Bernink PJ, McCabe CH, Horrowek T, Papuchis G, Mautner B, Corbalan R, Radley D, Braunwald E. The TIMI risk score for unstable angina/non-ST elevation MI: a method for prognostication and therapeutic decision making. *JAMA* 2000;284:835-42.
- Antman EM, McCabe CH, Gurfinkel EP, Turpie AG, Bernink PJ, Salein D, Bayes de Luna A, Fox K, Lablanche

- JM, Radley D, Premmereur J, Braunwald E. *Enoxaparin prevents death and cardiac ischemic events in unstable angina/non-Q-wave myocardial infarction: results of the thrombolysis in myocardial infarction (TIMI) 11B trial.* *Circulation* 1999;100:1593-601.
- 23) Cohen M, Demers C, Gurfinkel EP, Turpie AG, Fromell GJ, Goodman S, Langer A, Califf RM, Fox KA, Premmereur J, Bigonzi F. *A comparison of low-molecular-weight heparin with unfractionated heparin for unstable coronary artery disease.* *N Engl J Med* 1997;337:447-52.
  - 24) Cannon CP, Weintraub WS, Demopoulos LA, Vicari R, Frey MJ, Lakkis N, Neumann FJ, Robertson DH, DeLucca PT, DiBattiste PM, Gibson CM, Braunwald E. *Comparison of early invasive and conservative strategies in patients with unstable coronary syndromes treated with the glycoprotein IIb/IIIa inhibitor tirofiban.* *N Engl J Med* 2001;344:1879-87.
  - 25) Morrow DA, Antman EM, Snapinn SM, McCabe CH, Theroux P, Braunwald E. *An integrated clinical approach to predicting the benefit of tirofiban in non-ST elevation acute coronary syndromes: application of TIMI risk score for UA/NSTEMI in PRISM-PLUS.* *Eur Heart J* 2002;23:223-9.
  - 26) Braunwald E, Mark DB, Jones RH. *Unstable angina: diagnosis and management.* Rockville, MD: Agency for health care policy and research and the national, heart, lung, and blood institute, US public health service, US department of health and human service;1994:1. AHCPR Publication 94-0602.
  - 27) Katz DA, Griffith JL, Beshansky JR, Selker HP. *The use of empiric clinical data in the evaluation of practice guidelines for unstable angina.* *JAMA* 1996;276:1568-74.
  - 28) Hochman JS, Sleeper LA, Godfrey E, McKinlay SM, Sanborn T, Col J, LeJemtel T. *Should we emergently revascularize occluded coronaries for cardiogenic shock: an international randomized trial of emergency PTCA/ CABG-trial design.* *Am Heart J* 1999;137:313-21.
  - 29) Holmes DR Jr, Berger BP, Hochman JS, Granger CB, Thompson TD, Califf RM, Vahanian A, Bates ER, Topol EJ. *Cardiogenic shock in patients with acute ischemic syndromes with and without ST-segment elevation.* *Circulation* 1999;100:2067-73.
  - 30) Selker HP, Zalenski RJ, Antman EM, Aufderheide TP, Bernard SA, Bonow RO, Gibler WB, Hagen MD, Johnson P, Lau J, McNutt RA, Ornato J, Schwartz JS, Scott JD, Tunick PA, Weaver WD. *An evaluation of technologies for identifying acute cardiac ischemia in the emergency department.* *Ann Emerg Med* 1997;29:13-87.
  - 31) Rouan GW, Lee TH, Cook EF, Brand DA, Weisberg MC, Goldman L. *Clinical characteristics and outcome of acute myocardial infarction in patients with initially normal or nonspecific electrocardiograms.* *Am J Cardiol* 1989;64:1087-92.
  - 32) Savonitto S, Ardissino D, Granger CB, Morando G, Prando MD, Mafrici A, Cavallini C, Melandri G, Thompson TD, Vahanian A, Ohman EM, Califf RM, van de Werf F, Topol EJ. *Prognostic value of the admission electrocardiogram in acute coronary syndromes.* *JAMA* 1999;281:707-13.
  - 33) Lee TH, Cook EF, Weisberg MC, Rouan GW, Brand DA, Goldman L. *Impact of the availability of a prior electrocardiogram on the triage of the patient with acute chest pain.* *J Gen Intern Med* 1990;5:381-8.
  - 34) Fesmire FM, Percy RF, Wears RL. *Diagnostic and prognostic importance of comparing the initial to the previous electrocardiogram in patients admitted for suspected acute myocardial infarction.* *South Med J* 1991;84:841-6.
  - 35) Matetzky S, Freimark D, Feinberg MS, Novikov I, Rath S, Rabinowitz B, Kaplinsky E, Hod H. *Acute myocardial infarction with isolated ST-segment elevation in posterior chest leads V7-9: "hidden" ST-segment elevations revealing acute posterior infarction.* *J Am Coll Cardiol* 1999;34:748-53.
  - 36) de Zwaan C, Bar FW, Janssen JH, Cheriex EC, Dassen WR, Brugada P, Penn OC, Wellens HJ. *Angiographic and clinical characteristics of patients with unstable angina showing an ECG pattern indicating critical narrowing of the proximal LAD coronary artery.* *Am Heart J* 1989;117: 657-65.
  - 37) Slater DK, Hlatky MA, Mark DB, Harrell FE Jr, Pryor DB, Califf RM. *Outcome in suspected acute myocardial infarction with normal or minimally abnormal admission electrocardiographic findings.* *Am J Cardiol* 1987;60: 766-70.
  - 38) Cannon CP, McCabe CH, Stone PH, Rogers WJ, Schachtman M, Thompson BW, Pearce DJ, Diver DJ, Kells C, Feldman T, Williams M, Gibson RS, Kronenberg MW, Ganz LI, Anderson HV, Braunwald E. *The electrocardiogram predicts one-year outcome of patients with unstable angina and non-Q wave myocardial infarction.* *J Am Coll Cardiol* 1997;30:133-40.
  - 39) Ohman EM, Armstrong PW, Christenson RH, Granger CB, Katus HA, Hamm CW, O'Hanesian MA, Wagner GS, Kleiman NS, Harrell FE Jr, Califf RM, Topol EJ. *Cardiac troponin T levels for risk stratification in acute myocardial ischemia.* *N Engl J Med* 1996;335:1333-41.
  - 40) Antman EM, Tanasijevic MJ, Thompson B, Schachtman M, McCabe CH, Cannon CP, Fischer GA, Fung AY, Thompson C, Wybenga D, Braunwald E. *Cardiac-specific troponin I levels to predict the risk of mortality in patients with acute coronary syndromes.* *N Engl J Med* 1996;335:1342-9.
  - 41) Hyde TA, French JK, Wong CK, Straznicki IT, Whitlock RM, White HD. *Four-year survival of patients with acute coronary syndromes without ST-segment elevation and prognostic significance of 0.5 mm ST-segment depression.* *Am J Cardiol* 1999;84:379-85.
  - 42) Kudenchuk PJ, Maynard C, Cobb LA, Wirkus M, Martin JS, Kennedy JW, Weaver WD. *Utility of the prehospital electrocardiogram in diagnosing acute coronary syndromes: the myocardial infarction triage and intervention (MITI) project.* *J Am Coll Cardiol* 1998;32:17-27.
  - 43) Langer A, Freeman MR, Armstrong PW. *ST segment shift in unstable angina: pathophysiology and association with coronary anatomy and hospital outcome.* *J Am Coll Cardiol* 1989;13:1495-502.
  - 44) Langer A, Freeman MR, Armstrong PW. *Relation of angiographic detected intracoronary thrombus and silent myocardial ischemia in unstable angina pectoris.* *Am J Cardiol* 1990;66:1381-2.
  - 45) Hedges JR, Young GP, Henkel GF, Gibler WB, Green TR, Swanson JR. *Serial ECGs are less accurate than serial CK-MB results for emergency department diagnosis of myocardial infarction.* *Ann Emerg Med* 1992;21:1445-50.
  - 46) Patel DJ, Holdright DR, Knight CJ, Mulcahy D, Thakrar B, Wright C, Sparrow J, Wicks M, Hubbard W, Thomas R,

- Sutton GC, Hendry G, Purcell H, Fox K. *Early continuous ST segment monitoring in unstable angina: prognostic value additional to the clinical characteristics and the admission electrocardiogram.* *Heart* 1996;75:222-8.
- 47) Patel DJ, Knight CJ, Holdright DR, Mulcahy D, Clarke D, Wright C, Purcell H, Fox KM. *Long-term prognosis in unstable angina: the importance of early risk stratification using continuous ST-segment monitoring.* *Eur Heart J* 1998;19:240-9.
  - 48) Ellis AK. *Serum protein measurements and the diagnosis of acute myocardial infarction.* *Circulation* 1991;83:1107-9.
  - 49) Wu AH, Apple FS, Gibler WB, Jesse RL, Warshaw MM, Valdes R Jr. *National academy of clinical biochemistry standards of laboratory practice recommendations for the use of cardiac markers in coronary artery diseases.* *Clin Chem* 1999;45:1104-21.
  - 50) Roberts R, Fromm RE. *Management of acute coronary syndromes based on risk stratification by biochemical markers: an idea whose time has come.* *Circulation* 1998;98:1831-3.
  - 51) Adams JE 3rd, Abendschein DR, Jaffe AS. *Biochemical markers of myocardial injury: is MB creatine kinase the choice for the 1990s?* *Circulation* 1993;88:750-63.
  - 52) Mair J, Morandell D, Genser N, Lechleitner P, Dienstl F, Puschendorf B. *Equivalent early sensitivities of myoglobin, creatine kinase MB mass, creatine kinase isoform ratios, and cardiac troponin I and T for acute myocardial infarction.* *Clin Chem* 1995;41:1266-72.
  - 53) Puleo PR, Meyer D, Wathen C, Tawa CB, Wheeler S, Hamburg RJ, Ali N, Obermueller SD, Triana JF, Zimmerman JL. *Use of rapid assay of subforms of creatine kinase-MB to diagnose or rule out acute myocardial infarction.* *N Engl J Med* 1994;331:561-6.
  - 54) Hamm CW, Goldmann BU, Heeschen C, Kreymann G, Berger J, Meinertz T. *Emergency room triage of patients with acute chest pain by means of rapid testing for cardiac troponin T or troponin I.* *N Engl J Med* 1997;337:1648-53.
  - 55) Antman EM, Grudzien C, Mitchell RN, Sacks DB. *Detection of unsuspected myocardial necrosis by rapid bedside assay for cardiac troponin T.* *Am Heart J* 1997;133:596-8.
  - 56) Apple FS, Falahati A, Paulsen PR, Miller EA, Sharkey SW. *Improved detection of minor ischemic myocardial injury with measurement of serum cardiac troponin I.* *Clin Chem* 1997;43:2047-51.
  - 57) Pettijohn TL, Doyle T, Spiekerman AM, Watson LE, Riggs MW, Lawrence ME. *Usefulness of positive troponin-T and negative creatine kinase levels in identifying high-risk patients with unstable angina pectoris.* *Am J Cardiol* 1997;80:510-1.
  - 58) Galvani M, Ottani F, Ferrini D, Ladenson JH, Destro A, Baccos D, Rusticali F, Jaffe AS. *Prognostic influence of elevated values of cardiac troponin I in patients with unstable angina.* *Circulation* 1997;95:2053-9.
  - 59) Lindahl B, Andren B, Ohlsson J, Venge P, Wallentin L. *Risk stratification in unstable coronary artery disease: additive value of troponin T determinations and pre-discharge exercise test.* *Eur Heart J* 1997;18:762-70.
  - 60) Hamm CW, Heeschen C, Goldmann B, Vahanian A, Adgey J, Miguel CM, Rutsch W, Berger J, Kootstra J, Simoons ML. *Benefit of abciximab in patients with refractory unstable angina in relation to serum troponin T levels.* *N Engl J Med* 1999;340:1623-9.
  - 61) Heeschen C, Hamm CW, Goldman B, Deu A, Langenbrink L, White HD. *Troponin concentrations for stratification of patients with acute coronary syndromes in relation to therapeutic efficacy of tirofiban.* *Lancet* 1999;354:1757-62.
  - 62) Lindahl B, Venge P, Wallentin L. *Troponin T identifies patients with unstable coronary artery disease who benefit from long-term antithrombotic protection.* *J Am Coll Cardiol* 1997;29:43-8.
  - 63) Kontos MC, Anderson FP, Schmidt KA, Ornato JP, Tatum JL, Jesse RL. *Early diagnosis of acute myocardial infarction in patients without ST-segment elevation.* *Am J Cardiol* 1999;83:155-8.
  - 64) Zaninotto M, Altinier S, Lachin M, Celegon L, Plebani M. *Strategies for the early diagnosis of acute myocardial infarction using biochemical markers.* *Am J Clin Pathol* 1999;111:399-405.
  - 65) Kontos MC, Anderson FP, Hanbury CM, Roberts CS, Miller WG, Jesse RL. *Use of the combination of myoglobin and CK-MB mass for the rapid diagnosis of acute myocardial infarction.* *Am J Emerg Med* 1997;15:14-9.
  - 66) Lindahl B, Venge P, Wallentin L. *Early diagnosis and exclusion of acute myocardial infarction using biochemical monitoring.* *Coron Artery Dis* 1995;6:321-8.
  - 67) Hamm CW, Braunwald E. *A classification of unstable angina revisited.* *Circulation* 2000;102:118-22.
  - 68) Ardissino D, Merlini PA, Gamba G, Barberis P, Demicheli G, Testa S, Colombi E, Poli A, Fetsiveau R, Monte-martini C. *Thrombin activity and early outcome in unstable angina pectoris.* *Circulation* 1996;93:1634-9.
  - 69) Becker RC, Cannon CP, Bovill EG, Tracy RP, Thompson B, Knatterud GL, Randall A, Braunwald E. *Prognostic value of plasma fibrinogen concentration in patients with unstable angina and non-Q-wave myocardial infarction (TIMI IIIB trial).* *Am J Cardiol* 1996;78:142-7.
  - 70) Morrow DA, Rifai N, Antman EM, Weiner DL, McCabe CH, Cannon CP, Braunwald E. *Serum amyloid A predicts early mortality in acute coronary syndromes: a TIMI11A substudy.* *J Am Coll Cardiol* 2000;35:358-62.
  - 71) Oltrona L, Ardissino D, Merlini PA, Spinola A, Chiodo F, Pezzano A. *C-reactive protein elevation and early outcome in patients with unstable angina pectoris.* *Am J Cardiol* 1997;80:1002-6.
  - 72) Biasucci LM, Vitelli A, Liuzzo G, Altamura S, Caligiuri G, Monaco C, Rebuzzi AG, Ciliberto G, Maseri A. *Elevated levels of interleukin-6 in unstable angina.* *Circulation* 1996;94:874-7.
  - 73) Haverkate F, Thompson SG, Pyke SD, Gallimore JR, Pepys MB. *Production of C-reactive protein and risk of coronary events in stable and unstable angina.* *Lancet* 1997;349:462-6.
  - 74) Morrow DA, Rifai N, Antman EM, Weiner DL, McCabe CH, Cannon CP, Braunwald E. *C-reactive protein is a potent predictor of mortality independently of and in combination with troponin T in acute coronary syndromes.* *J Am Coll Cardiol* 1998;31:1460-5.
  - 75) de Lemos JA, Morrow DA, Bentley JH, Omland T, Sabatine MS, McCabe CH, Hall C, Cannon CP, Braunwald E. *The prognostic value of B-type natriuretic peptide in patients*



- with acute coronary syndrome. *N Engl J Med* 2001;345:1014-21.
- 76) Gibbons RJ, Balady GJ, Beasley JW, Bricker JT, Duvernoy WF, Froelicher VF, Mark DB, Marwick TH, McCallister BD, Thompson PD Jr, Winters WL, Yanowitz FG, Ritchie JL, Gibbons RJ, Cheitlin MD, Eagle KA, Gardner TJ, Garson A Jr, Lewis RP, O'Rourke RA, Ryan TJ. *ACC/AHA guidelines for exercise testing. J Am Coll Cardiol* 1997;30:260-311.
  - 77) Cheitlin MD, Alpert JS, Armstrong WF, Aurigemma GP, Beller GA, Bierman FZ, Davidson TW, Davis JL, Douglas PS, Gillam LD. *ACC/AHA guidelines for the clinical application of echocardiography. Circulation* 1997;95:1686-744.
  - 78) Ritchie JL, Bateman TM, Bonow RO, Crawford MH, Gibbons RJ, Hall RJ, O'Rourke RA, Parisi AF, Verani MS. *Guidelines for the clinical use of cardiac radionuclide imaging. J Am Coll Cardiol* 1995;25:521-47.
  - 79) Mark DB, Shaw L, Harrell FE Jr, Hlatky MA, Lee KL, Bengtson JR, McCants CB, Califf RM, Pryor DB. *Prognostic value of a treadmill exercise score in outpatients with suspected coronary artery disease. N Engl J Med* 1991; 325:849-53.
  - 80) Starling MR, Crawford MH, Kennedy GT, O'Rourke RA. *Treadmill exercise tests predischARGE and six weeks post-myocardial infarction to detect abnormalities of known prognostic value. Ann Intern Med* 1981;94:721-7.
  - 81) Marwick TH, Anderson T, Williams MJ, Haluska B, Melin JA, Pashkow F, Thomas JD. *Exercise echocardiography is an accurate and cost-efficient technique for detection of coronary artery disease in women. J Am Coll Cardiol* 1995;26:335-41.
  - 82) Russo CA, Dai H, Chow BK. *Analysis of death during the first twelve months among non-Q wave MI patients randomized to an "invasive" vs. "conservative" management strategy: results from the VANQWISH trial [Abstr]. Circulation* 1998;98 (Suppl 1):1492.
  - 83) Scanlon PJ, Faxon DP, Audet A, Carabello B, Dehmer GJ, Eagle KA, Legako RD, Leon DF, Murray JA, Nissen SE, Pepine CJ, Watson RM, Ritchie JL, Gibbons RJ, Cheitlin MD, Gardner TJ, Garson A Jr, Russell RO Jr, Ryan TJ, Smith SC Jr. *ACC/AHA guidelines for coronary angiography. J Am Coll Cardiol* 1999;33:1756-824.