In-hospital Outcome in Octogenarians with Acute Coronary Syndrome Undergoing Emergent Coronary Angiography

doi: 10.1536/jhj.44.11

In-hospital Outcome in Octogenarians with Acute Coronary Syndrome Undergoing Emergent Coronary Angiography

Kotaro OE,[1] MD, Masami SHIMIZU,[1] MD, Hidekazu INO,[1] MD, Masato YAMAGUCHI,[1] MD, Hidenobu TERAI,[1] MD, Kenshi HAYASHI,[1] MD, Masaru KIYAMA,[1] MD, Kenji SAKATA,[1] MD, Tatsumi HAYASHI,[1] MD, Masaru INOUE,[1] MD, Tomoya KANEDA,[1] MD, *and* Hiroshi MABUCHI,[1] MD

SUMMARY

Very elderly patients have higher mortality rates than younger patients after acute coronary syndrome (ACS). However, the mechanism by which increasing age contributes to such mortality remains unclear. In addition, the efficacy and safety of invasive coronary procedures for octogenarians with ACS have not been well established.

We compared the clinical characteristics and in-hospital outcome of 193 octogenarians (mean age, 83 years) with those of 1,462 younger patients (mean age, 64 years) with ACS who underwent emergent coronary angiography. Octogenarians included a greater number of females, had higher rates of cerebrovascular disease and multivessel disease, a higher Killip class, a higher Forrester class, and lower rates of smoking, diabetes, and hypercholesterolemia than the younger subjects. Interventions, including percutaneous transluminal coronary angioplasty (PTCA) and coronary artery bypass grafting (CABG), were performed less frequently in octogenarians than in younger patients (88.0% versus 90.8%). The procedural success rate in octogenarians did not differ from that in younger patients. However, the in-hospital mortality rate for the octogenarians was about three times higher than for the younger patients (19.2% versus 6.9%). Multivariate analysis revealed that the predictors of in-hospital mortality in the octogenarians were a higher Killip class and a higher Forrester class.

Octogenarians with ACS had fewer coronary risk factors and a similar success rate for the intervention, but had more greatly impaired hemodynamics and higher in-hospital mortality than the younger patients. Therefore, impaired myocardial reserve may contribute to a large portion of in-hospital deaths in octogenarians with ACS. (Jpn Heart J 2003; 44: 11-20)

Key words: Acute coronary syndrome, Octogenarian, Coronary angiography

From [1] Molecular Genetics of Cardiovascular Disorders, Division of Cardiovascular Medicine, Graduate School of Medical Science, Kanazawa University, Kanazawa, Japan.

Address for correspondence: Masami Shimizu, MD, Molecular Genetics of Cardiovascular Disorders, Division of Cardiovascular Medicine, Graduate School of Medical Science, Kanazawa University, Takara-machi 13-1, Kanazawa 920-8640, Japan.

Received for publication April 1, 2002.

Revised and accepted June 13, 2002.

INCREASING age is associated with higher mortality following acute coronary syndrome (ACS).[1-4] However, the mechanism by which increasing age contributes to mortality remains unknown. In addition, the therapeutic strategies for elderly patients have not been well established. Although thrombolytic therapy has been shown to improve survival in the elderly,[5,6] several studies have shown that primary percutaneous transluminal coronary angioplasty (PTCA) is superior for elderly patients.[1-3,7] However, the safety and efficacy of invasive coronary procedures (angiography, PTCA, and coronary artery bypass grafting (CABG)) are unclear in very elderly patients. As life expectancy continues to increase, we expect to encounter a significant increase in the number of patients with ACS who are at least 80 years old. Therefore, we investigated the clinical characteristics and in-hospital outcome in octogenarians with ACS who had undergone emergent coronary angiography.

METHODS

Patients: We retrospectively analyzed the data of 1,655 consecutive patients who presented with ACS, including myocardial infarction and unstable angina, and had undergone emergent coronary angiography between January 1995 and December 1999 at the hospitals participating in this study. Electrocardiographic criteria included persistent or transient ST elevation or a depression of more than 0.5 mm. Acute myocardial infarction (AMI) was considered to have occurred if the level of creatine kinase MB isoenzyme was above normal and comprised at least 3 percent of the total creatine kinase level. If the creatine kinase MB level had not been measured, the total creatine kinase level had to be more than twice the upper limit of the normal range. Significant stenosis was defined as a ≥75% reduction in coronary artery diameter. Procedural success of PTCA was defined as achieving stenosis of less than 75% of the residual diameter with Thrombolysis In Myocardial Infarction (TIMI) trial grade 3 flow. A bleeding complication was defined as an intracranial hemorrhage or severe bleeding requiring a blood transfusion.

Statistical analysis: The clinical characteristics and in-hospital outcome were compared between the octogenarian cohort and patients less than 80 years old. In-hospital mortality was the primary end-point. Statistical testing was performed using the chi-square test for categorical variables and the *t* test for continuous variables. We subsequently performed multivariate logistic regression analysis for in-hospital deaths along with variables that were significant in the univariate analysis. A P value <0.05 was considered statistically significant.

RESULTS

Baseline characteristics: The baseline clinical characteristics of the patients are presented in Table I. Of the 1655 consecutive patients, 1,462 (88%) were less than 80 years old (mean 63 years) and 193 patients (12%) were greater than 80 years old (mean 83 years). Octogenarians were more likely to be women and had a higher rate of prior cerebrovascular disease, a higher Killip class, and a higher Forrester class at presentation (Table I). Coronary risk factors such as diabetes, smoking, and hypercholesterolemia were less common and diastolic blood pres-

Table I. Baseline Characteristics of Patients Studied

	Age≥80 (n=193)	Age<80 (n=1462)	*P* value
Age (year)	83.4±2.8	63.5±10.2	<0.0001
Female sex	56.5	21.5	<0.0001
Myocardial infarction (%)	86.9	81.4	NS
Unstable angina (%)	13.1	18.6	
ST elevation (%)	78.9	72.6	NS
Hypertension (%)	52.9	44.4	NS
Diabetes (%)	27.6	34.1	0.0146
Smoking (%)	28.6	59.5	<0.0001
Hypercholesterolemia (%)	25.3	36.9	0.0062
Prior myocardial infarction (%)	13.2	10.4	NS
Prior angina (%)	36.1	38.3	NS
Prior congestive heart failure (%)	6.3	3.8	NS
Cerebrovascular disease (%)	17.3	9.4	0.0035
Prior CABG (%)	1.1	2.3	NS
Prior PTCA (%)	2.1	7.3	0.0245
Peripheral vascular disease (%)	3.7	2.7	NS
Heart rate (beats/min)	78.3±20.5	77.8±19.7	NS
Systolic blood pressure (mmHg)	128.6±29.7	129.5±27.4	NS
Diastolic blood pressure (mmHg)	68.5±14.5	74.6±29.6	0.0062
Killip class (%)			0.0010
1	116 (60.1)	1009 (69.0)	
2	16 (8.3)	77 (5.3)	
3	8 (4.1)	31 (2.1)	
4	19 (9.89)	63 (4.3)	
unknown	34 (17.6)	282 (19.3)	
			<0.0001
Forrester class (%)			
1	47 (24.4)	472 (32.3)	
2	21 (10.9)	140 (9.6)	
3	17 (8.8)	38 (2.6)	
4	15 (7.8)	23 (1.6)	
unknown	93 (48.2)	789 (54.0)	

sure was lower in the octogenarians. On the other hand, heart rate and systolic blood pressure did not differ between the two groups.

Angiographic characteristics and intervention: The octogenarians had a higher rate of multivessel disease. There were no significant differences in the prevalence of left main lesions or culprit lesions between the two groups (Table II). Interventions, including PTCA and CABG, were performed in 88.0% of the octogenarians and 90.8% of the younger patients. Thus interventions were performed less frequently in octogenarians than in younger patients (P=0.0104). The rate of procedural success was 89.8% in the octogenarians and 93.2% in the younger patients, which did not differ significantly (Table III).

Outcome: The older the patient, the higher the rate of in-hospital mortality (Figure 1). The in-hospital mortality rate was about three times higher in the octogenarians than in the younger patients (19.2% versus 6.9%), and the rate of bleeding complications was six times higher (3.9% versus 0.6%). The rate of recurrent

Table II. Angiographic Characteristics of Patients Studied

	Age≥80 (n=193)	Age<80 (n=1462)	*P* value
No. of diseased vessels (%)			0.0296
0	1.0	2.3	
1	38.3	47.7	
2	30.1	27.8	
3	29.5	20.9	
unknown	1.0	1.3	
Left main coronary disease (%)	4.7	3.5	NS
Culprit lesion * (%)			
Anterior descending	44.3	53.4	NS
Circumflex	18.2	12.6	
Right	37.5	34.0	

* Culprit lesions were assessed when patients had one vessel disease.

Table III. Clinical Outcome

Outcome	Age≥80 (n=%)	Age<80 (n=%)	Odds Ratio (95% CI)	*P* value
Death	37/193 (19.2)	101/1462 (6.9)	3.20 (2.12-4.82)	<0.0001
Procedural success	123/137 (89.8)	967/1038 (93.2)	0.65 (0.35-1.18)	NS
Bleeding complication	6/154 (3.9)	7/1113 (0.6)	6.45 (2.14-19.61)	0.0022
Recurrent ischemic event	16/154 (10.4)	83/1115 (7.4)	1.44 (0.82-2.53)	NS

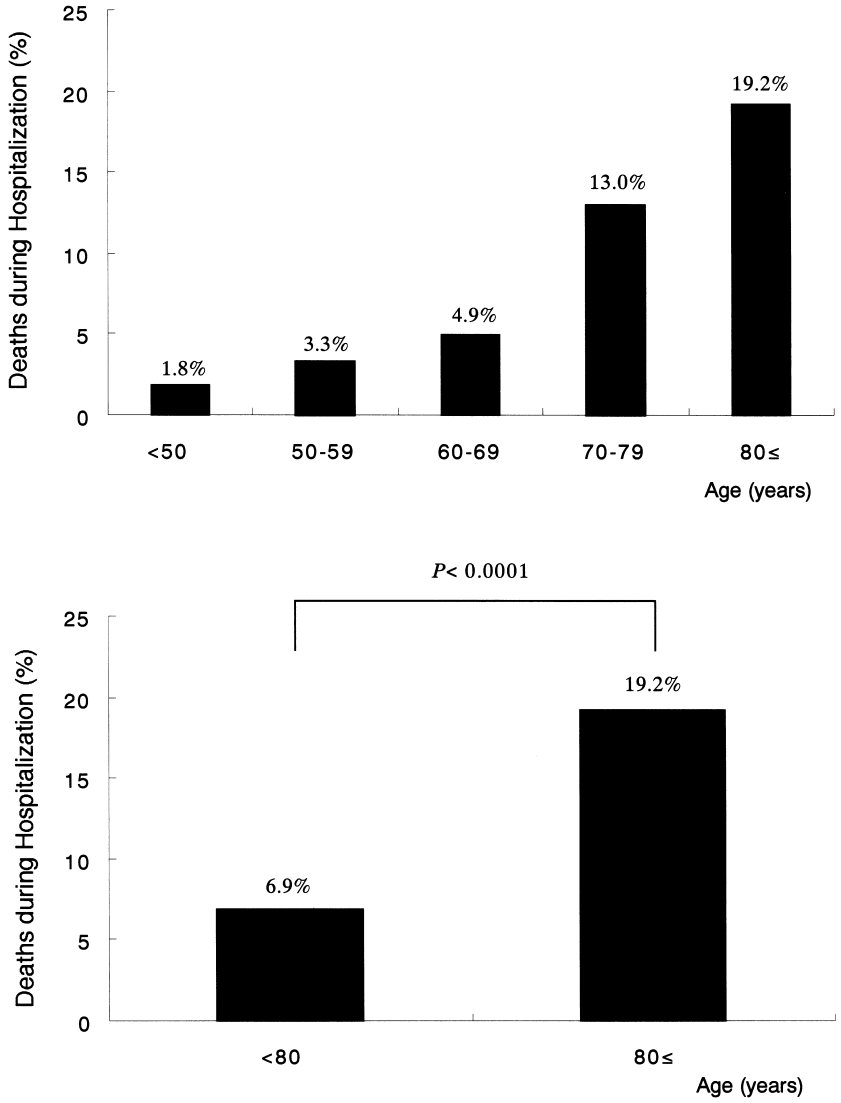

Figure 1. Rates of death during hospitalization for acute coronary syndrome according to age.

ischemic events between the two groups did not differ (Table III). The octogenarians had a higher in-hospital mortality rate with any type of ACS than the younger patients (Figure 2). Of the deaths, 60.6% occurred within 7 days, 85.6% within 35 days, and the others after 35 days.

Cause of death: Of the deaths, about half were due to heart failure, and the causes of death were not different between the two groups (Table IV). Other

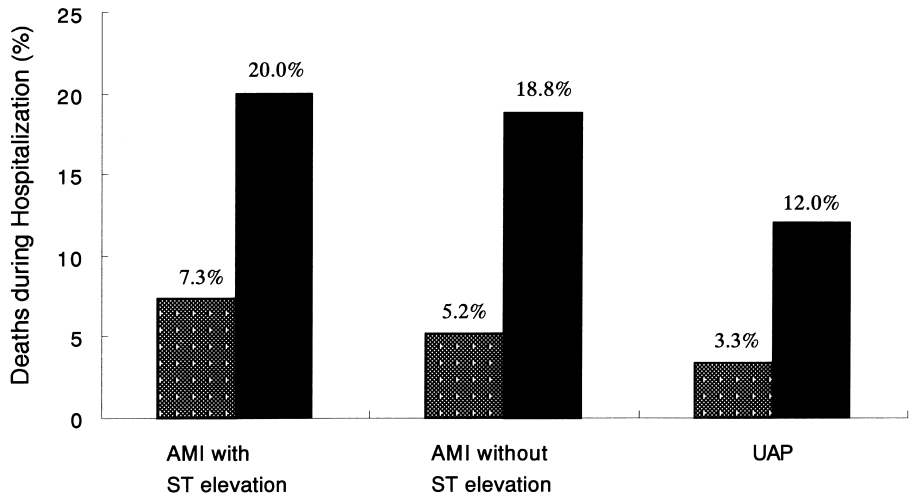

Figure 2. Rates of death during hospitalization for acute coronary syndrome (ACS) among octogenarians and younger patients, according to type of ACS. Gray bar, younger patients; black bar, octogenarians. AMI=acute myocardial infarction; UAP=unstable angina pectoris.

Table IV. Cause of Death

	Age≥80 (n=193)	Age<80 (n=1462)	*P* value
Cause of death-n (%)			NS
Heart failure	18 (48.6)	53 (52.5)	
Arrhythmia	3 (8.1)	10 (9.9)	
Other	5 (13.5)	15 (14.9)	
Unknown	11 (29.7)	23 (22.8)	

causes of death included cardiac rupture (8 cases), pneumonia (6 cases), renal failure (2 cases), cardiac tamponade with unknown cause (1 case), hepatic failure (1 case), mesenteric artery embolus (1 case), and disseminated intravascular coagulation (1 case).

Predictors of in-hospital mortality among octogenarians: Among the octogenarians, univariate analysis revealed that predictors of in-hospital mortality were greater age, lower systolic blood pressure, higher Killip class, and higher Forrester class (Table V). In multivariate analysis, only a higher Killip class (P=0.003) and higher Forrester class (P=0.046) remained as independent predictors of in-hospital mortality.

Table V. Univariate Predictors of In-hospital Mortality

Variables	Odds Ratio (95% CI)	*P* value
Age (/year)	1.17 (1.03-1.32)	0.0138
SBP (/mmHg)	0.98 (0.97-0.99)	0.0016
Killip class		
I	1	
II	8.10 (2.34-28.02)	
III	4.50 (0.78-26.01)	<0.0001
IV	29.25 (8.78-97.59)	
Forrester class		
I	1	
II	4.84 (0.41-56.65)	
III	19.17 (2.04-179.91)	0.0005
IV	23.00 (2.42-219.00)	

SBP=sytolic blood pressure

DISCUSSION

Previously reported reasons for increased mortality among elderly patients were multifactorial, including a high prevalence of comorbidity,[8,9] more diffuse multivessel disease,[4,8,10] delayed presentation,[11] greater risk of cardiac rupture,[12] insufficient use of beta-blocker[13] and aspirin,[14] and less aggressive treatment.[15] In this study, in-hospital mortality in the octogenarians with ACS was about three times higher than in the younger patients in spite of a similar rate of successful intervention. This suggests that impaired myocardial reserve and other comorbid conditions contributed to the worse prognosis among the octogenarians. There were no differences in the causes of in-hospital death between the two groups, suggesting that octogenarians have higher mortality from both cardiac decompensation and noncardiac multisystem dysfunction. The greater prevalence of multivessel disease and impaired myocardial reserve may be the cause of the more greatly impaired hemodynamics among the older patients. The major factors contributing to dysfunction of the aging heart are a decreased beta-sympathetic response and increased impedance to left ventricular ejection.[16] Moreover, the aging heart with its modest hypertrophy and consequent prolonged relaxation is perhaps more sensitive to ischemic injury with more profound consequences.[16]

Although reperfusion therapy reduces the infarction area and preserves left ventricular function, most clinicians are reluctant to use thrombolytic therapy in the elderly for fear of serious hemorrhagic complications.[11] Primary angioplasty has higher rates of vessel patency and TIMI grade 3 flow relative to thrombolytic therapy.[17] Therefore, to preserve cardiac function and improve prognosis, angioplasty should be the treatment of choice in octogenarians with ACS. In fact, sev-

eral studies have shown a lower mortality rate when elderly patients are treated with primary PTCA compared with thrombolytic therapy.[1-3,7] The Fibrinolytic Therapy Trialists (FTT) overview[18] showed that the rate of death during days 0 - 35 in patients ≥75 years old with AMI was 24.3% in the fibrinolytic group and 25.3% in control patients. Other previous studies reported that mortality reaches ≥30% in octogenarian patients with AMI.[2,9,12] In this study, in-hospital mortality of the octogenarians with AMI was 19.9%. This suggests that emergent coronary angiography and subsequent intervention may be superior to thrombolysis and routine therapy with antiplatelet agents and heparin alone.

In this study, the octogenarians had about a six times higher rate of bleeding complications than the younger patients (3.7% versus 0.6%), which was higher than that reported in the FTT overview (fibrinolytic group, 1.1%; control, 0.5%).[18] However, we suppose that most of the bleeding complications were access site complications and invasive coronary procedures (angiography and intervention) are relatively safe even in octogenarians.

There is a prevailing notion that the strength of the association of cardiovascular risk factors with the development of coronary heart disease diminishes with advancing age.[19] Consistent with this notion, octogenarians in this study had fewer coronary risk factors, including diabetes, smoking, and hypercholesterolemia. This suggests that very great age in itself is a risk factor of coronary artery disease, and the cause of poor hemodynamics. In this study, poor hemodynamics strongly predict in-hospital death in octogenarians. Therefore, octogenarians who have a high Killip class or high Forrester class require more careful management.

Study limitations: This study has several limitations. First, it was not randomized, and information on the octogenarians for whom emergent coronary angiography was not performed is lacking. Therefore, octogenarians in this study may have had fewer comorbid conditions than those in whom emergent coronary angiography was not performed. Second, we did not determine the prevalence of thrombolytic therapy among these patients, which is a principal therapy for AMI in Western populations. Although the exact prevalence is not known, we feel that the number of patients who received thrombolytic therapy was very small in this study. Third, the prevalence of aspirin, beta-blocker, and angiotensin converting enzyme inhibitor use, which reduces the mortality after AMI,[20] was not determined. Fourth, we did not consider PTCA and CABG separately, but rather combined them as one intervention type. Therefore, the prevalence of each therapy among these patients is unknown.

Conclusions: Although there were no significant differences in the rate of success of the intervention, the octogenarians had more greatly impaired hemodynamics and higher in-hospital mortality than the younger patients. We suppose that impaired myocardial reserve contributes to a large portion of in-hospital

deaths and aggressive recanalization strategies (emergent coronary angiography and subsequent intervention) may be effective in improving the prognosis of octogenarians with ACS.

ACKNOWLEDGMENT

We are grateful to the follwing participating institutions and chief investigators of the Hokuriku ACS Study Group for their support in this study: Ishikawa Prefecture Central Hospital (H. Kanaya, B. Kaku); Kaga Central Hospital (Y. Kita); Kanazawa Social Insurance Hospital (M. Minamoto, M. Nagata); Kanazawa Cardiovascular Hospital (M. Namura, T. Tsuchiya); Keijyu General Hospital (Y. Horita); Koseiren Takaoka Hospital (K Shimizu); Komatsu City Hospital (K. Ueda.); Saiseikai Kanazawa Hospital (T. Araki, T. Konno); Shinminato City Hospital (N. Takeda); Tatsunokuchi Hoju Memorial Hospital (S. Mori); Toyama Red Cross Hospital (Y. Nitta); Himi City Hospital (K. Misawa); Fukui Prefecture Hospital (J. Hirai); Hokuriku Hospital (H. Oiwake); Yokohama Sakae Kyosai Hospital (I. Michishita, T. Iwaki).

REFERENCES

1. Stone GW, Grines CL, Browne KF, *et al*. Predictors of in-hospital and 6-month outcome after acute myocardial infarction in the reperfusion era: the primary angioplasty in myocardial infarction (PAMI) trial. J Am Coll Cardiol 1995; 25: 370-7.
2. Holmes DR, White HD, Pieper KS, *et al*. Effect of age on outcome with primary angioplasty versus thrombolytics. J Am Coll Cardiol 1999; 33: 412-9.
3. Gusto IIb Angioplasty Substudy Investigators. A clinical trial comparing primary coronary angioplasty with tissue plasminogen activator for acute myocardial infarction. N Engl J Med 1997; 336: 1621-8.
4. DeGeare VS, Stone GW, Grines L, *et al*. Angiographic and clinical characteristics associated with increased in-hospital mortality in elderly patients with acute myocardial infarction undergoing percutaneous intervention. Am J Cardiol 2000; 86: 30-4.
5. Topol EJ, Califf RM. Thrombolytic therapy for elderly patients. N Engl J Med 1992; 327: 45-7.
6. Gurwitz JH, Goldberg RJ, Gore JM. Coronary thrombolysis for the elderly? JAMA 1991; 265: 1720-3.
7. Arai S, Awaya T, Aono J, *et al*. Efficacy of primary percutaneous transluminal coronary angioplasty for acute myocardial infarction in patients aged ≥80 years. J Cardiol 2000; 35(5): 335-41.
8. Smith SC, Gilpin E, Ahnve S, *et al*. Outlook after acute myocardial infarction in the very elderly compared with that in patients aged 65 to 70 years. J Am Coll Cardiol 1990; 16: 784-92.
9. Weaver WD, Litwin PE, Martin JS, *et al* for the MITI Project Group. Effect of age on use of thrombolytic therapy and mortality in acute myocardial infarction. J Am Coll Cardiol 1991; 18: 657-62.
10. Tofler GH, Muller JE, Stone PH, *et al* and MILIS Study Group. Factors leading to shorter survival after acute myocardial infarction in patients aged 65 to 75 years compared with younger patients. Am J Cardiol 1988; 62: 860-7.
11. Holmes DR. Dilatation versus thrombolytic therapy in elderly patients. In: Wenger NK, editor. *Cardiovascular Disease in the Octogenarian and Beyond*. London: Martin Dunitz 1999; 205-13.
12. Maggioni AP, Maseri A, Fresco C, *et al* for the Gruppo Italiano per lo Studio Della Sopravivenza nell'Infarto Miocardico (GISSI-2). Age related increase in mortality among patients with first myocardial infarction related with thrombolysis. N Engl J Med 1993; 329: 1442-8.

13. Gurwitz JH, Goldberg RJ, Chen Z, Gore JM, Alpert JS. β-blocker therapy in acute myocardial infarction: evidence for underutilization in the elderly. Am J Med 1992; 93: 605-10.
14. Krumholtz HM, Radford MJ, Ellerbeck EF, *et al*. Aspirin in the treatment of acute myocardial infarction, 1988 to 1992. Circulation 1995; 92: 2841-7.
15. Taddei CFG, Weintraub WS, Shaw L, Kosinski AS. Coronary angioplasty and other transcatheter revascularization procedures. In: Wenger NK, editor. *Cardiovascular Disease in the Octogenarian and Beyond*. London: Martin Dunitz 1999; 185-204.
16. Edward GL, Gary G, Myron LW. The aging heart: structure, function, and disease. In: Braunwald E, editor. *Heart Disease: A Textbook of Cardiovascular Medicine*, Fifth Edition. Philadelphia: W.B. Saunders Company, 1997: 1687-703.
17. Grines CL. Should thrombolysis or primary angioplasty be the treatment of choice for acute myocardial infarction? N Engl J Med 1996; 335: 1311-7.
18. Fibrinolytic Therapy Trialist' (FTT) Collaborative Group. Indication for fibrinolytic therapy in suspected acute myocardial infarction: collaborative overview of early mortality and major morbidity results from all randomised trials of more than 1000 patients. Lancet 1994; 343: 311-22.
19. Kannel WB, Wilson PWF, Larson MG, Evans JC. Coronary risk factors and coronary prevention in octogenarians. In: Wenger NK, editor. *Cardiovascular Disease in the Octogenarian and Beyond*. London: Martin Dunitz 1999; 141-63.
20. ACC/AHA guidelines for management of patients with acute myocardial infarction. J Am Coll Cardiol 1996; 28: 1328-428.