Myocardial infarction with normal coronary arteries: ten-year follow-up

Pier-Giorgio Golzio, Fulvio Orzan, Paolo Ferrero, Marco Bobbio, Serena Bergerone, Margherita Di Leo, Gian Paolo Trevi

Cardiology, Department of Internal Medicine, University of Turin, Turin, Italy

Key words:
Atherosclerosis; Coronary angiography; Coronary arteries; Follow-up; Myocardial infarction; Prognosis.

Background. **Patients with myocardial infarction without angiographically significant coronary artery lesions are considered, as a whole, to have a better prognosis. Different degrees of coronary involvement, within this wide group, may portend different degrees of risk. The aim of this study was to assess which clinical and angiographic covariates are more useful in defining the individual prognosis.**

Methods. **We prospectively followed 53 consecutive patients admitted to our coronary care unit between 1985-1990 with myocardial infarction and a culprit lesion causing ≤ 50% angiographic luminal narrowing.**

Results. **Patients with normal angiograms (group A) were compared to those with minor parietal irregularities (group B) or discrete (≤ 50%) stenosis (group C). Group A patients were younger, had a lower peak creatine kinase release, and a higher ejection fraction. After a median follow up of 125 ± 32 months, group A patients had a 100% 10-year survival compared to 77 and 58% for group B and group C patients respectively (p = 0.01). At univariate analysis, ischemic events correlated with the severity of coronary lesions (while group A patients had no ischemic events at follow-up, events occurred in 46 and 50% of group B and C patients respectively; p = 0.003) and with ejection fraction, that was lower in patients with events (56.0 ± 17 vs 67 ± 11%, p = 0.006). Cardiac death, too, correlated with the type of coronary lesions (p = 0.03) and with lower ejection fraction (p = 0.004). By means of multivariate analysis, on the contrary, only the vessel morphology was predictive of ischemic events at follow-up (p = 0.02), while the only significant predictor of death was ejection fraction (p = 0.0012).**

Conclusions. **Patients with myocardial infarction and strictly normal vessels have very few ischemic events at follow-up, and may be distinguished from both patients with non-significant lesions as well as those with minor angiographic irregularities. On the other hand, cardiac mortality correlates strongly and independently with a depressed ventricular function.**

(Ital Heart J 2004; 5 (10): 732-738)

Received May 31, 2004; revision received August 3, 2004; accepted August 24, 2004.

Address:

Dr. Pier-Giorgio Golzio

Cardiologia Universitaria Dipartimento di Medicina Interna Università degli Studi c/o Ospedale "Molinette" Corso A.M. Dogliotti, 14 10126 Torino E-mail: pgolzio@molinette.piemonte.it

Introduction

Normal coronary arteries have been described in 1-12% of all infarcts[1-12], with up to a 4 times greater prevalence among younger patients[6,8,13-18]. However, the accurate estimation of the so-called "infarct with normal coronary artery" is complicated by the different definitions of "normal" coronary arteries. In fact, in all the available literature, the label of non-obstructive coronary artery disease refers to a wide spectrum of angiographic findings, ranging from a strictly smooth contour of the vessel wall to a focal, > 70% stenosis, of a minor secondary branch of the coronary tree[19]. It is not surprising, indeed, that such a generic definition may be responsible for both the variability in the prevalence and in the clinical outcomes reported in studies dealing with normal coronary artery infarcts. It is well known that many acute coronary events occur in patients with non-critical and trivial coronary lesions. The clinical relevance of this feature has now become even greater, owing to the development of intravascular ultrasound technology, by means of which subtle pathological changes of the vessel wall may be disclosed[20]. While the role of conventional angiographic findings in assessing the prognosis of patients after a myocardial infarction is sound and well established, the evaluation of the coronary tree by intravascular ultrasound on a systematic basis has not yet been extensively validated. For this reason, further clarification of the prognostic relevance of the different patterns of atherosclerotic involvement of the coronary artery tree seems necessary. The aim of the present study was to re-assess the clinical features, in-hospital course, and late prognosis of patients with different angiographic patterns of the so-called "normal coronary arteries" after an acute myocardial infarction (AMI).

Methods

Population. We reviewed all the admissions to the coronary care unit of the University Hospital, Turin, from 1985 to 1990. Eight hundred seventy-seven patients had a confirmed diagnosis of AMI[21,22] (692 males, 79%; 648 Q wave myocardial infarction, 74%). There were 114 in-hospital deaths (13%). Coronary angiography was performed during hospitalization in 404 (53%) of 762 survivors, and 53 patients (13.1%) were classified as having angiographically "normal coronary arteries".

Definitions and criteria. Coronary angiography was recommended in case of post-infarction angina and/or ischemia, complicated course, non-Q wave myocardial infarction (first infarct), and young age (≤ 40 years).

In all patients multiple views of the coronary arteries were obtained and the ejection fraction was calculated. The coronary angiographies were analyzed by three of the authors according to the method of independent observers, and depending on the type of coronary lesions, three groups were defined:
- group A: strictly normal coronary arteries, i.e. no irregularity of the wall contour;
- group B: minor irregularities, i.e. small, diffuse abnormalities of the coronary lumen profile, without a discrete filling defect;
- group C: non-significant lesions, i.e. discrete narrowing ≤ 50%.

Follow-up. We followed all the patients of the original study group either by regular follow-up visits, or through telephone interviews. The mean follow-up was 125 ± 32 months. The occurrence of the following events was investigated further: angina, myocardial infarction, coronary revascularization by means of percutaneous transluminal coronary angioplasty or coronary artery bypass grafting, and death (sudden, cardiac, non-cardiac).

Data analysis. Categorical variables were compared using the χ^2 test or the Fisher's exact test, as appropriate. Continuous variables were compared using the Student's t-test for non-paired data. Comparison among three or more groups was analyzed by means of one-way ANOVA analysis, applying the Bonferroni test for associations within groups. Whenever a statistically significant difference was found, differences between paired groups were evaluated using the Pearson t-test. With regard to univariate/multivariate analysis, the following variables were included: sex, coronary risk factors, age at infarction, thrombolytic treatment, Q wave myocardial infarction, peak creatine kinase release, angiographic type of coronary abnormality, ejection fraction. The relative risk was calculated. A stepwise logistic regression model (forward conditional) was used. In our model, we separately considered all the events and cardiac death as the dependent variable, and included as covariates those variables which showed a statistically significant difference at univariate analysis.

Kaplan-Meier cumulative survival curves were plotted for survival, cardiac survival, and event-free survival. Log-rank, Breslow and Tarone-Ware tests were used to assess the differences between the cumulative survivals.

The results were considered statistically significant for p values ≤ 0.05.

Statistical analysis was performed using SPSS statistical software, 11.5 release (SPSS Inc., Chicago, IL, USA).

Results

Study population. The demographic characteristics and coronary risk factors were similar in patients with "normal coronary arteries" as a whole (i.e. with coronary lesions ≤ 50%) and in those with at least one lesion > 50% (Table I), with the exception of age at the time of infarction, which was younger in the former group.

Comparison of groups A, B and C (Table II). A strictly normal coronary angiogram was found in 16 patients (group A); minor irregularities were diagnosed in 13 (group B), and discrete non-significant stenoses were found in 24 (group C). Group A patients were significantly younger, had a lower peak creatine kinase release, and a better ejection fraction than those in groups B and C. The prevalence of diabetes, hypercholesterolemia, hypertension, current smoking and of a family history of coronary artery disease did not significantly differ among the three groups.

Follow-up. After 10 years, all group A patients were alive compared with 10 of 13 group B and 14 of 24 group C patients (77 and 58% respectively). Cardiac or sudden death was observed in 2 of 13 group B vs 8 of 24 group C patients, with a statistically relevant difference (Table III). Moreover, group A patients had sig-

Table I. Comparison of patients with "normal" (with ≤ 50% culprit stenosis) and diseased (with > 50% culprit stenosis) coronary arteries.

	Stenosis ≤ 50%	Stenosis > 50%	p
No. patients	53	351	
Male sex	43 (81%)	288 (82%)	NS
Age at AMI (years)	45.5 ± 11.6	58 ± 9	< 0.0001
Hypercholesterolemia	16 (30%)	147 (42%)	NS
Hypertension	22 (42%)	149 (42%)	NS
Smoking	34 (64%)	263 (72%)	NS
Family history	15 (28%)	91 (26%)	NS
Diabetes mellitus	2 (4%)	42 (12%)	NS

AMI = acute myocardial infarction.

Table II. Comparison of the patients with "normal" coronary arteries: groups A, B and C. Epidemiology and clinical features of acute myocardial infarction (AMI).

	Group A (n=16)	Group B (n=13)	Group C (n=24)	p
Male sex	13 (81%)	8 (62%)	22 (92%)	NS
Age at AMI (years)	37.2 ± 13.1	51.8 ± 7.9	47.6 ± 9.3	0.0009 A vs B
Angina before AMI	4 (25%)	1 (8%)	7 (29%)	NS
Peak CK (IU/l)	591 ± 265	777 ± 434	1439 ± 1243	0.009 A vs C
Thrombolysis	9 (56%)	6 (46%)	10 (40%)	NS
Extension	0	1 (8%)	4 (17%)	
EF (%)	72 ± 10	63 ± 17	59 ± 13	0.02 A vs C

CK = creatine kinase; EF = ejection fraction.

Table III. Events at follow-up.

	Group A (n=16)	Group B (n=13)	Group C (n=24)	p
Follow-up (months)	133.2 ± 23.9	126.5 ± 30.8	118.1 ± 37.2	NS
Total mortality	0	3 (23%)	10 (42%)	0.011
Cardiac and sudden death	0	2 (15%)	8 (33%)	0.029
All events*	0	6 (46%)	12 (50%)	0.003

* all events include cardiac and sudden deaths, post-infarction angina, new acute myocardial infarction, heart failure, coronary artery bypass graft.

nificantly less events (none vs 46% in group B patients and 50% in group C) (Table III). None of our patients underwent coronary angioplasty or coronary artery bypass grafting. At Kaplan-Meier analysis, the actuarial event-free survival was 133 ± 24 months for group A patients, 117 ± 21 months for group B, and 111 ± 16 months for group C (p = 0.006). Figure 1 shows the actuarial event-free survival curve of group A, B and C patients. The survival free of cardiac death was 120 ± 16 months for patients with ejection fraction < 50%, and 184 ± 74 months for patients with ejection fraction ≥ 50% (p < 0.005). Figure 2 shows the actuarial survival curves of 44 patients with ejection fraction ≥ 50% and of 9 patients with ejection fraction < 50%.

Univariate analysis. The results of univariate analysis are shown in tables IV and V.

Predictors of events. Angiographic abnormalities of the coronary vessels, older age, and lower ejection fraction

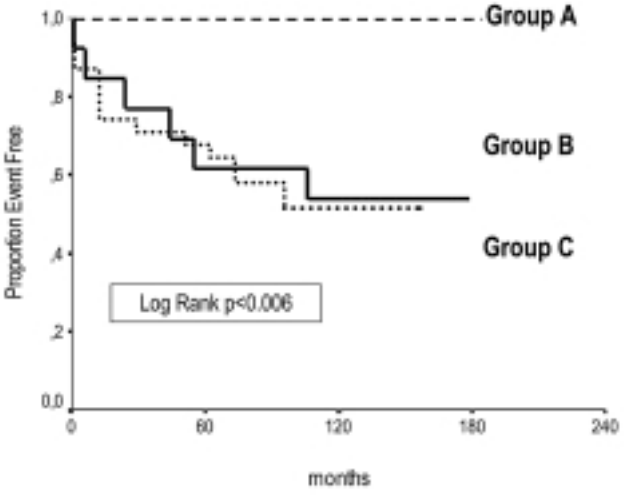

Figure 1. *Actuarial event-free survival for patients of study group A (strictly normal coronary arteries), B (minor irregularities of the wall contour) and C (discrete, non-significant narrowing ≤ 50%).*

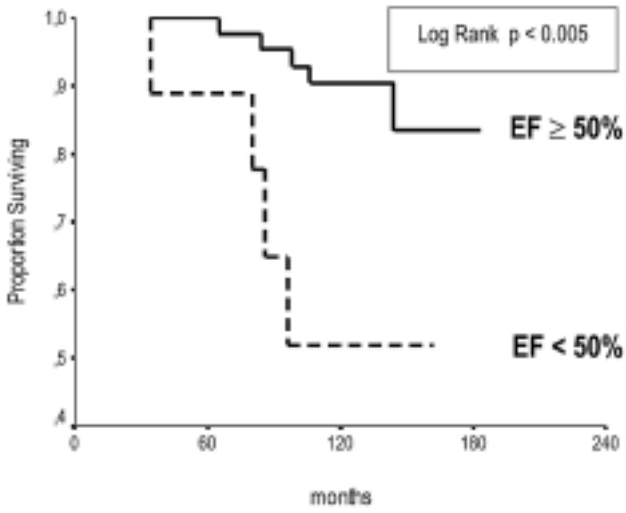

Figure 2. *Actuarial survival of patients with ejection fraction (EF) < 50% vs ≥ 50%.*

Table IV. Univariate analysis. Total events vs event-free.

	With events (n=18)	Event-free (n=35)	p	RR (odds ratio)	95% CI
Coronary lesions			0.003	–	–
Group A	0	16 (46%)			
Group B	6 (33%)	7 (20%)			
Group C	12 (67%)	12 (34%)			
Male sex	16 (89%)	27 (77%)	NS	2.1	0.5-8.7
Age at AMI (years)	51 ± 9	43 ± 12	0.017	–	–
Family history	7 (39%)	8 (23%)	NS	1.2	0.8-1.9
Anterolateral AMI	12 (67%)	16 (46%)	NS	1.6	0.8-3.3
Q wave AMI	11 (61%)	22 (63%)	NS	1.1	0.4-1.9
No thrombolysis	12 (67%)	16 (46%)	NS	1.6	0.8-3.3
Peak CK (IU/l)	1078 ± 1173	959 ± 803	NS	–	–
EF (%)	56 ± 17	67 ± 11	0.006	–	–

AMI = acute myocardial infarction; CI = confidence interval; CK = creatine kinase; EF = ejection fraction; RR = relative risk.

Table V. Univariate analysis. Cardiac mortality vs alive.

	Cardiac mortality (n=10)	Alive or non-cardiac death (n=43)	p	RR (odds ratio)	95% CI
Coronary lesions			0.03	–	–
Group A	0	16 (37%)			
Group B	2 (20%)	11 (27%)			
Group C	8 (80%)	16 (37%)			
Male sex	10 (100%)	33 (77%)	NS	1.3	1.1-1.5
Age at AMI (years)	52 ± 11	44 ± 11	0.017	–	–
Family history	3 (30%)	12 (28%)	NS	1.1	0.2-5
Anterolateral AMI	8 (80%)	20 (46%)	0.056	3.6	0.8-15.3
Q wave AMI	7 (70%)	26 (60%)	NS	1.5	0.3-6.7
No thrombolysis	9 (90%)	19 (44%)	0.009	1.4	1.1-1.8
Peak CK (IU/l)	1086 ± 1460	980 ± 790	0.056	–	–
EF (%)	51 ± 20	66 ± 11	0.004	–	–

AMI = acute myocardial infarction; CI = confidence interval; CK = creatine kinase; EF = ejection fraction; RR = relative risk.

were significantly associated with the occurrence of events at univariate analysis (Table IV).

Predictors of cardiac death. At univariate analysis, cardiac mortality was significantly associated with coronary angiographic abnormalities, older age, no thrombolysis in the acute setting, and lower ejection fraction (Table V).

Multivariate analysis. At multivariate analysis, only the angiographic morphology of the coronary vessel was found to be significantly predictive of events (p = 0.0238; Table VI), while the only significant predictor of death was the ejection fraction (p = 0.0012; Table VI).

Discussion

The occurrence of an AMI in a patient without evidence of coronary artery disease is well known. The rate of such an event accounts for 1 up to 12% of all myocardial infarctions. These figures are even higher if only AMI occurring before the age of 40 (the so-called "juvenile" AMI) are considered, increasing to 22% for males and 34% for females. These prevalence data have been extrapolated from those of the CASS Registry[23,24].

To the best of our knowledge, two main theories have been proposed in an attempt to explain these syndromes: endothelial dysfunction triggered by an inflammatory pathway, and coronary spasm, possibly superimposed on a trivial coronary stenosis. Cigarette smoking has been viewed as a possible trigger of an acute ischemic syndrome, by eliciting a sustained coronary spasm[12,19,25-27]. However, this mechanism has not been always demonstrated in the clinical setting[28], and neither can we confirm a higher prevalence of cigarette smoking among our patients.

Acquired or, more frequently, congenital defects of the coagulation pathway have been sometimes identified, but are not so common in clinical practice. Our

Table VI. Multivariate analysis. Method: stepwise logistic regression, forward conditional.

Covariates	Initial significance, model z^2		Term removed	Significance, model z^2	Residual covariates	Significance, model z^2	
	Total equation	Single covariate					
Dependent variable: ischemic events							
Group of coronary lesions (A, B, C)	0.0314	0.0227	Group	0.0238	EF	0.1755	
EF		0.0262					
						Total equation	Single covariate
Dependent variable: cardiac death							
Group of coronary lesions (A, B, C)	0.012	0.50	EF	0.0012	Group	0.9286	0.9
Peak CK		0.000			Peak CK		0.96
EF		0.0004					
EF < 50%		0.018			EF < 50%		0.19

AMI = acute myocardial infarction; CK = creatine kinase; EF = ejection fraction.

study is a follow-up study based on historical data (retrospective analysis of case records and coronary angiographies). For this reason, an etiological evaluation is beyond the scope of the present article.

Nowadays, however, the most likely explanation for the occurrence of AMI in the absence of detectable atherosclerotic disease relies on the well recognized inaccuracy of coronary angiography in detecting subtle changes of the vessel wall that could be responsible for an acute thrombosis of the lumen. The use of intravascular ultrasound allowed the identification of anatomical changes in the coronary artery wall even in angiographically normal segments[29,30]. Nevertheless, coronary angiography remains a pivotal diagnostic and prognostic tool. In fact, as previously described[31], the extension and seriousness of the angiographic findings, graded according to the classical criteria, is strongly related to the presence of thrombogenic wall lesions. In other words, the more extensive the angiographically detected atherosclerotic burden, the higher the chances of finding complex, unstable, although not obstructive, lesions.

From the clinical point of view, patients with angiographically normal coronary arteries are younger, have better systolic and diastolic ventricular functions, and their AMI is often the first clinical manifestation of ischemic disease, not being preceded nor followed by angor, while there are no significant differences in the infarction site[32]. In our study, we were able to confirm that patients who are found to have a stenosis ≤ 50% are significantly younger but we could not confirm a lower prevalence of the conventional cardiovascular risk factors.

As for the prognosis, it is well known that patients without significant organic stenosis fare better than those with definite coronary artery disease. This finding is partly dependent on the other features described above, such as age and systolic function. Previous works have variably defined globally normal coronary arteries as those with no stenosis at all[10], with stenoses < 25%[18], < 30%[7,12,21,23], and < 50%[6,9,21,26,27]. Owing to this, the rate of major ischemic events was 20% after 3 years in the work of Pecora et al.[33]. Similarly, the mortality rates ranged from 0% at 2[6] and 4 years[12], to 2.5% at 1.5 years[9], 5% at 5 years[23], and 15% at 10.5 years[18]. Our follow-up data referring to the study population as a whole show a 34% event rate and a 19% mortality rate at 10 years and are hence comparable with those reported by other authors. The slight discrepancy with our results seems to be due to the different inclusion criteria (that is, the percent of luminal narrowing taken as the cut-off point between "normal" and "diseased" coronary arteries), and perhaps to the criteria employed for coronary angiography, which was employed more frequently over time. Still, the analyses performed in the present study clearly identify a better prognosis for patients with strictly normal coronary arteries, and a worse follow-up status for patients with even trivial coronary artery involvement. Hence, our finding that group A patients are totally free of ischemic events and of cardiac death, whereas group B and C patients present with definite ischemic events (46 and 50% respectively) and with cardiac death (23 and 42%) seems more accurate.

Thus, a more accurate distinction on the basis of even relatively minor angiographic differences seems warranted. With regard to this, Proudfit et al.[34] had already shown in 1980 that the 10-year survival was significantly better (93.6 vs 74.6%) in patients with lesions < 30% (normal and mild narrowing) compared to

those with a 30-50% stenosis (moderate narrowing). Moreover, even a retrospective analysis performed by Ziemmerman et al.[19] on 8839 patients included in the CASS registry confirms a significantly higher survival rate in the group with a normal angiography (91 vs 75% during a 7-year time span). On the other hand, in this study the presence of detectable, albeit not hemodynamically significant, coronary artery disease portends a higher risk of reinfarction (16 vs 5% in the group with strictly normal coronary arteries, during a 7-year follow-up). Interestingly, studies comparing angiographies performed after a second myocardial infarction clearly disclose that most reinfarctions are due to the abrupt occlusion of a coronary artery tract which had been seen to be characterized by just subtle parietal changes at the first diagnostic study[28,34,35].

As for the prognostic role of left ventricular dysfunction, its significance with respect to mortality is emphasized in a more recent prospective study. This study confirms the known better event-free survival of patients with a strictly smooth vascular contour as compared to those with > 50% coronary artery stenosis (75% event-free survival at 35 months vs 61%)[32]. However, at the same time it also highlights that the mortality does not significantly differ among the two groups, whereas left ventricular systolic function and diabetes mellitus turn out to be the only two independent variables correlated with death.

Study limitations. Our study is a prospective study based on historical data. Our population was defined in 1990 by retrospective analysis of case records and review of coronary angiographies. From then on, we prospectively followed our population at regular outpatient visits.

The study population is quite small but is all the same comparable to, or even greater than, those reported in the recent literature[28,32].

We did not perform a Cox proportional hazard regression model analysis. However, to the best of our knowledge, our study is the only one which analyzes survival using the Kaplan-Meier method.

We also analyzed risk factor modification throughout the follow-up period, and the related medications prescribed. However, we chose not to report these results in the present study because we think that ischemic events and death provide the strongest statistical arguments when evaluating follow-up data.

The concept that even mild coronary lesions may pose a risk of subsequent coronary event is well accepted, although still debated[36]. However, the only study that followed ischemic patients over a comparably long time is that of Proudfit et al.[34]. In spite of the fact that even this latter study proved this assumption, it unfortunately only included patients with suspected coronary disease, and not with a diagnosed myocardial infarction; moreover, the follow-up period (1970-1980) clearly precedes the widespread use of thrombolysis, aspirin, beta-blockers and ACE-inhibitors, that are now held to be the mainstay of the management of ischemic patients.

In conclusion, our study clearly shows that patients with "normal" or "near-normal" coronary arteries (our three A, B, C patient groups: with strictly normal coronary arteries, with minor irregularities of the wall contour and with ≤ 50% lesions respectively) differ significantly. As a matter of fact, multivariate analysis and cumulative survival analysis confirmed that a depressed left ventricular function is the only independent predictor of cardiac death. As far as ischemic events are concerned, only strictly normal coronary arteries appear to have an ischemia-free survival, whereas the angiographic finding of even minimal coronary lesions is significantly related to the occurrence of events. In this regard, it should be noted that minor irregularities of the wall contour have the same prognostic value as discrete non-significant lesions.

Thus, after a myocardial infarction, patients with minimal irregularities of the wall contour need careful follow-up and secondary prevention, even though in the absence of a depressed left ventricular function their cardiac mortality will be low.

References

1. Alpert JS. Myocardial infarction with angiographically normal coronary arteries: a personal perspective. (editorial) Arch Intern Med 1994; 154: 245.
2. Campeau L, Lesperance J, Bourassa MG, Ashekian PB. Myocardial infarction without obstructive disease at coronary arteriography. Can Med Assoc J 1968; 99: 837-43.
3. Bruschke AV, Bruyneel KJ, Bloch A, van Herpen G. Acute myocardial infarction without obstructive coronary artery disease demonstrated by selective cinearteriography. Br Heart J 1971; 33: 585-94.
4. Khan AH, Haywood LJ. Myocardial infarction in nine patients with radiographically patent coronary arteries. N Engl J Med 1974; 291: 427-31.
5. Bertrand ME, Lefebvre JM, Laisne CL, Rousseau MF, Carre AG, Lekrieffe JP. Coronary arteriography in acute transmural myocardial infarction. Am Heart J 1979; 97: 61-9.
6. Betriu A, Pare JC, Sanz G, et al. Myocardial infarction with normal coronary arteries: a prospective clinical-angiographic study. Am J Cardiol 1981; 48: 28-31.
7. Legrand V, Deliege M, Henrard L, Boland J, Kulbertus H. Patients with myocardial infarction and normal coronary arteriograms. Chest 1982; 82: 678-85.
8. Hoit BD, Gilpin EA, Henning H, et al. Myocardial infarction in young patients: an analysis by age subsets. Circulation 1986; 74: 712-21.
9. Kereiakes DJ, Topol EJ, George BS, et al. Myocardial infarction with minimal coronary atherosclerosis in the era of thrombolytic reperfusion. The Thrombolysis and Angioplasty in Myocardial Infarction (TAMI) Study Group. J Am Coll Cardiol 1991; 17: 304-12.
10. Vassanelli C, Menegatti G, Zanotto G, et al. L'infarto miocardico a coronarie angiograficamente normali. Cardiologia 1991; 36 (Suppl 1): 161-70.

11. Brecker SJ, Stevenson RN, Roberts R, Uthayakumar S, Timmis AD, Balcon R. Acute myocardial infarction in patients with normal coronary arteries. BMJ 1993; 307: 1255-6.
12. Sharifi M, Frohlich TG, Silverman IM. Myocardial infarction with angiographically normal coronary arteries. Chest 1995; 107: 36-40.
13. Thompson SI, Vieweg WV, Alpert JS, Hagan AD. Incidence and age distribution of patients with myocardial infarction and normal coronary arteriograms. Cathet Cardiovasc Diagn 1977; 3: 1-9.
14. Glover MU, Kuber MT, Warren SE, Vieweg WV. Myocardial infarction before age 36: risk factors and arteriographic analysis. Am J Cardiol 1982; 49: 1600-3.
15. Puel J, Massabuau P, Cassagneau B. Myocardial infarction before the age of 35. Clinical and coronarographic aspects. Presse Med 1983; 12: 1911-4.
16. Roskamm H, Gohlke H, Sturzenhofecker P, Samek L, Betz P. Myocardial infarction at a young age (under 40 years). Int J Sports Med 1984; 5: 1-9.
17. Weinberger I, Rotenberg Z, Fuchs J, Sagy A, Friedmann J, Agmon J. Myocardial infarction in young adults under 30 years: risk factors and clinical course. Clin Cardiol 1987; 10: 9-15.
18. Raymond R, Lynch J, Underwood D, Leatherman J, Razavi M. Myocardial infarction and normal coronary arteriography: a 10 year clinical and risk analysis of 74 patients. J Am Coll Cardiol 1988; 11: 471-7.
19. Ziemmerman FG, Cameron A, Fisher L, Grace NG. Myocardial infarction in young adults: angiographic characterization, risk factors and prognosis (Coronary Artery Surgery Study Registry). J Am Coll Cardiol 1995; 26: 654-61.
20. Hodgson JM, Reddy KG, Suneja R, Nair NR, Lesnefsky EJ, Sheehan HM. Intracoronary ultrasound imaging correlation of plaque morphology with angiography, clinical syndrome and procedural results in patients undergoing coronary angioplasty. J Am Coll Cardiol 1993; 21: 35-44.
21. Ryan TJ, Anderson JL, Antman EM, et al. ACC/AHA guidelines for the management of patients with acute myocardial infarction: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on management of acute myocardial infarction). J Am Coll Cardiol 1996; 281: 1328-428.
22. Beta-Blocker Heart Attack Trial Research Group. A randomized trial of propranolol in patients with acute myocardial infarction. I. Mortality results. JAMA 1982; 247: 1707-14.
23. Ciraulo DA, Bresnahan GF, Frankel PS, Isely PE, Zimmerman WR, Chesne RB. Transmural myocardial infarction with normal coronary angiograms and with single vessel coronary obstruction. Clinical-angiographic features and five-year follow-up. Chest 1983; 83: 196-202.
24. Principal Investigators of CASS and their Associates. The National Heart, Lung and Blood institute. Coronary Artery Surgery Study (CASS). Circulation 1981; 63 (Suppl I): I1-I81.
25. Suggiishi M, Faminaro T. Cigarette smoking is a major risk factor for coronary spasm. Circulation 1993; 87: 76-9.
26. Ross R, Kay R, Ambrose J, Herman MV. Coronary thrombosis in the absence of angiographically-evident obstructive coronary disease. Chest 1983; 84: 768-70.
27. McKenna WJ, Chew CY, Oakley CM. Myocardial infarction with normal coronary angiogram. Possible mechanism of smoking risk in coronary artery disease. Br Heart J 1980; 43: 493-8.
28. Fournier JA, Sanchez-Gonzalez A, Quero J, et al. Normal angiogram after myocardial infarction in young patients. A prospective clinical-angiographic and long-term follow-up study. Int J Cardiol 1997; 60: 281-7.
29. Caussin C, Ohanessian A, Lancelin B, et al. Coronary plaque burden detected by multislice computed tomography after acute myocardial infarction with near normal coronary arteries by angiography. Am J Cardiol 2003; 92: 849-52.
30. Glagov S, Weisenberg E, Zarins CK, Stankunavicius R, Kolettis GJ. Compensatory enlargement of various human atherosclerotic coronary arteries. N Engl J Med 1987; 316: 1371-5.
31. Mintz GS, Painter JA, Pichard AD, et al. Atherosclerosis in angiographically "normal" coronary artery reference segments: an intravascular ultrasound study with clinical correlations. J Am Coll Cardiol 1995; 25: 1479-85.
32. Da Costa A, Isaaz K, Faure E, Mourot S, Cerisier A, Lamaud M. Clinical characteristics, aetiological factors and long-term prognosis of myocardial infarction with an absolutely normal coronary angiogram. A 3-year follow-up study of 91 patients. Eur Heart J 2001; 22: 1459-65.
33. Pecora MJ, Roubin GS, Cobbs BW Jr, Ellis SG, Weintraub WS, King SB 3rd. Presentation and late outcome of myocardial infarction in the absence of angiographically significant coronary artery disease. Am J Cardiol 1988; 62: 363-7.
34. Proudfit WL, Bruschke AV, Sones FM Jr. Clinical course of patients with normal or slightly or moderately abnormal coronary arteriograms: 10-year follow-up of 521 patients. Circulation 1980; 62: 712-7.
35. Little WC, Constantinescu M, Applegate RJ, et al. Can coronary angiography predict the site of subsequent myocardial infarction in patients with mild-to moderate coronary artery disease? Circulation 1988; 78: 1157-66.
36. Jacq L, Chabredier-Paquot C, Pezzano M, et al. Prognostic value of normal coronary angiography. Ann Cardiol Angeiol (Paris) 2001; 50: 404-7.