# Influence of Revascularization on Long-Term Outcome in Patients ≥75 Years of Age With Diabetes Mellitus and Angina Pectoris

Raban V. Jeger, MD, Piero O. Bonetti, MD, Michael J. Zellweger, MD, Daniel Tobler, MD, Christoph A. Kaiser, MD, Stefan Osswald, MD, Peter T. Buser, MD, Matthias E. Pfisterer, MD*, and the TIME Investigators

**Little is known about the effect of revascularization in patients ≥75 years of age with symptomatic coronary artery disease (CAD) and diabetes mellitus (DM) for whom periprocedural risk and overall mortality are increased. Therefore, we examined the 301 patients of the Trial of Invasive versus Medical therapy in the Elderly with symptomatic CAD (TIME) with special regard to diabetic status. Patients were randomized to an invasive versus optimized medical strategy. The median follow-up was 4.1 years (range 0.1 to 6.9). Patients with DM (n = 69) had a greater incidence of hypertension (73% vs 58%, p = 0.03), ≥2 risk factors (93% vs 46%, p <0.01), previous heart failure (22% vs 12%, p = 0.04), and previous myocardial infarction (59% vs 43%, p = 0.02), and a lower left ventricular ejection fraction (48% vs 54%, p = 0.02) than did patients without DM. Mortality was greater in patients with DM than in those without DM (41% vs 25%, p = 0.01; adjusted hazard ratio 1.86, p = 0.01). Revascularization improved the overall survival rate from 61% (no revascularization) to 79% (p <0.01; adjusted hazard ratio 1.68, p = 0.03), an effect similarly observed in patients with and without DM. The event-free survival rate was 11% in nonrevascularized patients with DM compared with 40% in nonrevascularized patients without DM and 41% and 53% in revascularized patients with and without DM, respectively (p <0.01). Angina severity and antianginal drug use were similar for patients with and without DM, but those with DM performed worse in daily activities and physical functioning. In conclusion, elderly diabetic patients with chronic angina have a worse outcome than those with DM but benefit similarly from revascularization regarding symptom relief and long-term outcome. However, physical functioning related to daily activities is reduced in those with DM and may need special attention.**

**(Am J Cardiol 2005;96:193–198)**

No data are available comparing medical and revascularization strategies in elderly patients with diabetes mellitus (DM) for whom the intervention risk is increased further and coronary artery disease (CAD) usually more diffuse. Moreover, it is not known whether elderly diabetic patients with CAD derive similar benefit from an invasive strategy as do younger patients. The Trial of Invasive versus Medical therapy in the Elderly with symptomatic CAD (TIME) was the first prospective study comparing 2 CAD treatment strategies in elderly patients.[1,2] It offered the opportunity to compare the effects of these treatment strategies in elderly patients with versus without DM and to evaluate whether revascularization should also be considered in diabetic patients ≥75 years of age.

## Methods

**Patients:** The TIME protocol has been previously described.[3] In brief, patients ≥75 years who were referred to 1 of 14 Swiss centers for assessment of chronic angina pectoris (Canadian Cardiovascular Society class ≥2), despite receiving ≥2 antianginal drugs, were enrolled irrespective of whether they had undergone previous revascularization procedures. Patients were excluded if they had acute myocardial infarction within the previous 10 days, concomitant valvular or other heart disease, predominant heart failure, life-limiting concomitant diseases such as cancer or severe renal failure, an unwillingness or impossibility to undergo revascularization, and an impossibility of increasing or optimizing medical therapy. The ethics committee of the Swiss Academy of Medical Sciences and the local ethics committees of each center approved the study. Each patient gave informed written consent. For the present analysis, all patients with known DM were compared with those without DM.

**Definitions and follow-up:** In this prespecified subgroup analysis, DM was defined as treatment with antidia-

Department of Cardiology, University Hospital, Basel, Switzerland.
Manuscript received December 23, 2004; revised manuscript received and accepted March 8, 2005.

This study was supported by the Swiss Heart Foundation, Bern, and Adumed Foundation, Zurich, Switzerland.
* Corresponding author: Tel: 41-61-265-52-14; fax: 41-61-265-45-98.
*E-mail address:* pfisterer@email.ch (M.E. Pfisterer).

0002-9149/05/$ – see front matter © 2005 Elsevier Inc. All rights reserved.
doi:10.1016/j.amjcard.2005.03.042

betic drugs and/or a history of DM. Patients were randomized to an invasive or optimal medical strategy. The invasive strategy consisted of coronary angiography in all patients, followed by percutaneous coronary intervention or coronary artery bypass graft surgery, if feasible, according to the decision of the physicians in the participating centers. The optimal medical strategy was an increase in the number and/or dose of antianginal drugs, with the aim to reduce symptoms as much as possible. Additionally, antithrombotic and lipid-lowering drugs were advised. Quality of life was assessed by a standardized questionnaire containing the Short Form 12,[4] the Duke Activity Status Index,[5] and the Rose Questionnaire for angina.[6] The primary end point was defined as quality of life and freedom from major adverse clinical events, that is, death, documented myocardial infarction, and hospital admission for acute coronary syndromes with or without the need for revascularization after 6 months. A follow-up examination was done after 6 and 12 months and by questionnaire after a median of 4.1 years (range 0.1 to 6.9) to obtain information on quality of life and the occurrence of death, myocardial infarction, and hospitalizations with or without revascularization.[7] All reported deaths were verified through death certificates or by review of hospital charts, and the reason of death was defined as cardiac or noncardiac. Myocardial infarction was defined as a clinical event with significant electrocardiographic and enzymatic changes. An independent event committee adjudicated all possible events for this study.

**Statistical analysis:** The study was designed as a multicenter-controlled randomized trial, and all statistical analyses were performed at the study center in Basel, Switzerland. Although the initial analysis was based on the intention-to-treat principle, this analysis was based on a secondary analysis according to the treatment-received principle. Continuous variables were described as the mean value and SD, and comparisons between groups were done with the Wilcoxon Mann-Whitney test. A comparison of categorical variables was performed using the chi-square test or Fisher's exact test. Time-to-event variables with censored values were described using Kaplan-Meier statistics, and comparisons between groups were assessed using the log-rank test or the Cox proportional hazards model, adjusting for baseline differences in gender, age, hypertension, previous myocardial infarction, previous congestive heart failure, peripheral vascular disease, and use of $\beta$-blockers, diuretics, and angiotensin-converting enzyme inhibitors. Quality-of-life questionnaires were analyzed according to the specific tests used, as previously described.[1] Because no significant long-term survival or quality-of-life differences were noted in the overall TIME study,[7] all antianginal therapies, drugs, and revascularizations were taken together in the present analysis of patients with versus without DM. All p values were 2-sided, and $p < 0.05$ was considered statistically significant.

Table 1
Baseline characteristics

| Variable | Diabetes Mellitus | | p Value* |
|---|---|---|---|
| | No (n = 232) | Yes (n = 69) | |
| Age (yrs) (mean ± SD) | 80 ± 4 | 80 ± 4 | 0.76 |
| Women | 44 | 41 | 0.57 |
| Systemic hypertension | 58 | 73 | 0.03 |
| Current smoker | 32 | 39 | 0.29 |
| History of hypercholesterolemia | 49 | 46 | 0.59 |
| ≥2 Atherosclerotic risk factors | 46 | 93 | <0.01 |
| Previous myocardial infarction | 43 | 59 | 0.02 |
| Previous percutaneous coronary intervention | 10 | 1 | 0.02 |
| Previous coronary artery bypass grafting | 12 | 9 | 0.49 |
| Dyspnea | 55 | 65 | 0.12 |
| Previous heart failure | 12 | 22 | 0.04 |
| Peripheral vascular disease | 14 | 29 | <0.01 |
| Renal failure | 11 | 17 | 0.15 |
| ≥2 Co-morbidities | 24 | 35 | 0.08 |
| Left ventricular ejection fraction (mean ± SD) | 0.54 ± 0.12 | 0.48 ± 0.12 | 0.02 |
| No. of coronary arteries narrowed >50%† | | | |
| 0 | 8 | 5 | 0.30 |
| 1 | 14 | 15 | |
| 2 | 20 | 13 | |
| 3 | 58 | 67 | |
| Drug therapy | | | |
| Acetylic salicylic acid | 84 | 82 | 0.75 |
| Warfarin derivatives | 11 | 16 | 0.22 |
| Diuretics | 35 | 52 | 0.01 |
| Angiotensin-converting enzyme inhibitors | 25 | 43 | <0.01 |
| $\beta$ blockers | 81 | 64 | <0.01 |
| Calcium antagonists | 49 | 54 | 0.44 |
| Long-acting nitrates | 74 | 83 | 0.14 |
| Molsidomin | 38 | 39 | 0.88 |
| Digoxin | 5 | 10 | 0.09 |
| Lipid-lowering agents | 24 | 24 | 0.99 |

* Wilcoxon Mann-Whitney test for continuous and Fisher's exact test for categorical variables.
† Known for invasive treatment–assigned patients only.

## Results

**Patients and baseline characteristics:** Of the 301 TIME patients, 69 (23%) had DM. Of the patients with DM, 18 (26%) were treated with insulin. Compared with the patients without DM, those with DM had increased cardiovascular morbidity but less often received adequate antiischemic therapy (Table 1). However, no significant baseline differences were noted regarding the number of angiographically diseased vessels (Table 1) or parameters of symptom severity or quality of life (Table 2) between those with and without DM. No significant differences in baseline characteristics existed between patients with DM with and without insulin therapy (data not shown).

**Revascularization during follow-up:** During follow-up, 46 patients with DM (67%) and 133 patients without DM (57%) underwent revascularization (p = 0.21), most

Table 2
Symptoms and quality of life

| | Diabetes mellitus | | p Value* |
|---|---|---|---|
| | No (n = 232) | Yes (n = 69) | |
| Angina | | | |
| CCS class (baseline) | 3.1 ± 0.7 | 3.2 ± 0.7 | 0.12 |
| CCS class (1 year) | 1.3 ± 1.6 | 1.6 ± 1.5 | 0.14 |
| CCS class (long-term) | 1.1 ± 1.5 | 1.5 ± 1.7 | 0.21 |
| Rose score (baseline) | 3.7 ± 1.0 | 3.4 ± 1.3 | 0.14 |
| Rose score (1 year) | 1.7 ± 1.9 | 2.4 ± 1.9 | 0.02 |
| Rose score (long-term) | 1.6 ± 1.9 | 2.2 ± 2.2 | 0.13 |
| Short Form 12 | | | |
| Physical (baseline) | 32.4 ± 10.2 | 32.2 ± 9.6 | 0.82 |
| Physical (one year) | 41.9 ± 9.4 | 40.1 ± 10.9 | 0.39 |
| Physical (long-term) | 41.5 ± 10.5 | 37.1 ± 10.6 | 0.07 |
| Mental (1 year) | 49.9 ± 11.3 | 50.1 ± 11.3 | 0.76 |
| Mental (1 year) | 52.6 ± 9.3 | 51.3 ± 8.3 | 0.29 |
| Mental (long-term) | 53.4 ± 8.3 | 49.7 ± 10.7 | 0.20 |
| Duke Activity Status Index | | | |
| Baseline | 13.3 ± 11.3 | 12.8 ± 11.7 | 0.58 |
| 1 year | 19.0 ± 14.2 | 14.3 ± 11.8 | 0.04 |
| Long-term | 18.5 ± 13.6 | 11.0 ± 12.4 | 0.0005 |

Data presented as mean ± SD.

CCS and Rose score 0 to 4, with 0 = no pain and 4 = pain at rest. Duke Activity Status Index scores on scale from 0 to 58, with higher scores indicating more favorable status. Short Form 12 scores on scale from 0 to 100, with higher scores indicating more favorable status.

* Wilcoxon Mann-Whitney test.

CCS = Canadian Cardiovascular Society class.

within the first year of the study (91% of diabetics and 99% of nondiabetic patients). Of all revascularized patients, 57% of those with and 62% of those without DM underwent revascularization by treatment assignment (invasive strategy group; p = 0.49), and 45% and 41%, respectively, did so for drug-refractory symptoms during the first year of follow-up (optimal drug strategy group; p = 0.69). In patients with DM, revascularization was performed by percutaneous coronary intervention in 30 (65%) and coronary artery bypass graft surgery in 16 (35%) compared with percutaneous coronary intervention in 81 (61%) and coronary artery bypass graft surgery in 52 (39%) without DM (p = 0.72; Figure 1).

**Long-term symptoms and quality of life:** Neither angina severity measured by Canadian Cardiovascular Society class and the Rose questionnaire score nor the mean number of antianginal drugs differed in patients with and without DM at long-term follow-up (Table 2). However, the ease of performing daily activities, as measured by the Duke Activity Status Index score, was significantly worse for patients with DM compared with those without DM, a finding supported by a trend toward worse physical functioning in patients with DM according to the Short Form 12 data. In contrast, no changes were observed over time and no differences were found between patient groups in the mental component summary score of Short Form 12.

**Long-term freedom from major events:** During follow-up, 28 patients with DM (41%) died compared with 57 (25%) without DM (p = 0.01; Table 3), a difference that remained significant after adjustment for baseline differences (adjusted hazard ratio 1.86, p = 0.01; Figure 2). A similar difference in disfavor of patients with DM was noted for the cardiac death rate (33% vs 18%, p = 0.01; adjusted hazard ratio 1.98, p = 0.02), but not for nonfatal cardiac events. Overall, freedom from major adverse clinical events after long-term follow-up was only 16% for patients with DM compared with 34% for patients without DM (p = 0.01; adjusted hazard ratio 1.33, p = 0.09). Of those with DM, patients requiring insulin treatment tended to have greater cardiac mortality than did those who did not or those without DM (39% vs 31% vs 18%, p = 0.02). The adjusted hazard ratio was 2.8 (p = 0.03) for patients with DM treated with insulin compared with patients without DM. The adjusted hazard ratio was 1.4 (p = 0.37) for patients with DM who did not require insulin compared with patients without DM.

**Effect of revascularization during first year on long-term events:** Overall, revascularization during the first year of the study had a beneficial effect on long-term survival. The survival rate with revascularization was 79% versus 61% without revascularization (p ≤0.01; adjusted hazard ratio 1.68, p = 0.03). This beneficial effect of revascularization on cardiac survival was also noted in patients with and without DM (Figure 3). The survival rate for those with DM was 74% versus 52% for those who underwent and did not undergo revascularization (p = 0.07), respectively. The survival rate for those without DM was 90% versus 72% for those who underwent and did not undergo revascularization (p <0.01; p for interaction = 0.21), respectively. Similarly, long-term survival without major adverse clinical events was greatest in nondiabetic patients with revascularization (53%) followed by patients with DM and revascularization (41%) and patients without DM on continued drug therapy (40%). These rates contrasted with the worst survival rate for patients with DM who did not undergo revascularization without major adverse clinical events of only 11% (p

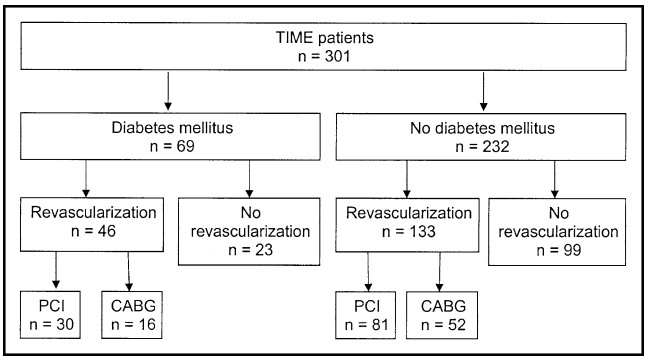


Figure 1. Flowchart of TIME patient population. CABG = coronary artery bypass graft surgery; PCI = percutaneous coronary intervention.

Table 3
Major adverse clinical events

| Event | Diabetes mellitus | | p Value* | HR† | p Value‡ |
|---|---|---|---|---|---|
| | No (n = 232) | Yes (n = 69) | | | |
| Any death | 25 | 41 | 0.01 | 1.86 | 0.01 |
| Cardiac death | 18 | 35 | 0.01 | 1.98 | 0.02 |
| Myocardial infarction | 13 | 9 | 0.40 | 0.44 | 0.11 |
| Revascularization | 27 | 32 | 0.40 | 1.21 | 0.48 |
| Hospitalization without revascularization | 27 | 22 | 0.45 | 1.15 | 0.60 |
| Major adverse clinical events | 66 | 84 | 0.01 | 1.33 | 0.09 |

* Fisher's exact test.
† Adjusted by gender, age, hypertension, previous myocardial infarction, previous congestive heart failure, peripheral vascular disease, and treatment with β-blockers, diuretics, and angiotensin-converting enzyme inhibitors.
‡ Cox proportional hazards model.
HR = hazard ratio.

≤0.01). Among the revascularized patients with DM, no significant differences were found in long-term outcome between the 2 methods of revascularization used. The mortality rates after percutaneous coronary intervention and coronary artery bypass graft surgery were similar in patients with (25% vs 43%, p = 0.32) and without (10% vs 19%, p = 0.22) DM. However, in patients with DM, angina was less severe at late follow-up (Rose score 0.9 ± 1.6 vs 2.6 ± 1.9, p = 0.04 for percutaneous coronary intervention and coronary artery bypass graft surgery, respectively) and drug use was lower (1.1 ± 0.3 vs 1.9 ± 1.1 for antianginal drugs, p <0.01) after surgery compared with after percutaneous coronary intervention.

## Discussion

The present analysis is the first study to address the effect of different anti-ischemic therapies on long-term outcome in patients ≥75 years with DM compared with those without DM of similar age. Our results have shown that both all-cause and cardiac survival are worse in elderly patients with DM, particularly if the patients require insulin. However, elderly patients with DM seem to benefit similarly from revascularization in terms of symptom relief and long-term cardiac survival compared with patients without DM. Still, physical functioning, particularly regarding daily activities, is reduced in patients with DM compared with those without DM. Physical function may need special attention in these elderly patients for them to keep their independence. This has been shown before for younger populations[8] and may in part be explained by the greater prevalence of co-morbidities and lower ejection fractions in patients with DM.

In younger populations, subgroup analyses comparing medical and revascularization strategies have suggested that symptomatic improvement is greater in patients with versus without DM after revascularization but that mortality is not

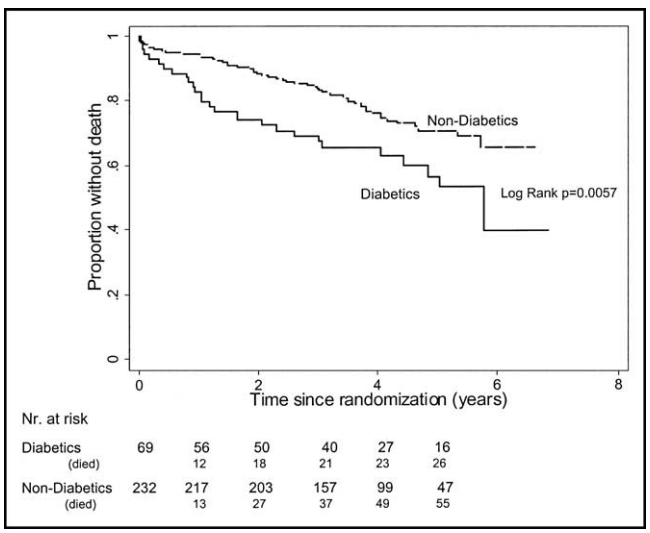


Figure 2. Kaplan-Meier survival curve (all-cause deaths) of TIME patients with versus without DM (log-rank p = 0.0057).

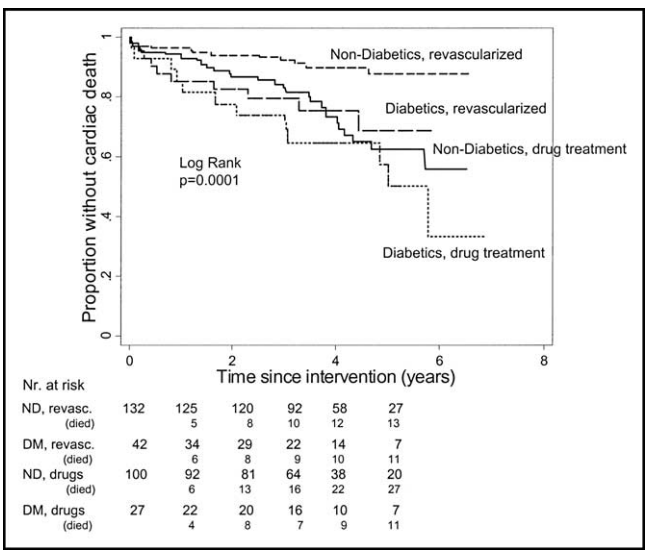


Figure 3. Kaplan-Meier survival curve (cardiac deaths) of TIME patients with versus without DM and with and without revascularization (log-rank p = 0.0001).

significantly different.[9] These findings are complicated by factors including that silent ischemia after revascularization is relatively frequent and that DM is an independent predictor of adverse events in patients after percutaneous coronary intervention.[10] Furthermore, silent ischemia in patients with DM has a prognostic input similar to that of symptomatic ischemia.[11] Until the present analysis, no data were available on the outcome of patients ≥75 years with DM regarding medical versus revascularization therapy, although DM and age have repeatedly been identified as independent risk factors of CAD.[12] The present findings have confirmed that mortality is particularly high in elderly patients with DM. Our results suggest, however, that these patients benefit similarly from revascularization as nondiabetic patients, not only in symptom relief, but also in long-term survival.

Despite the similar effects of the 2 anti-ischemic treatment strategies on angina severity in the total TIME population and in the subgroups of patients with and without DM, differences in quality of life existed between these 2 subgroups. During follow-up, patients with DM were more limited in their daily activities than were those without DM, as measured by the Duke Activity Status Index, and physical functioning tended to be more impaired in patients with DM, as measured by Short Form 12. Similar observations have not been previously published. These findings may be of major importance for elderly patients with DM, indicating that these patients may need particular help to maintain their independence. In contrast, their mental functioning did not seem to be limited compared with that of nondiabetic patients, and mental functioning did not appear to be influenced by anti-ischemic therapy.

The beneficial effect of revascularization on outcome in the present analysis was of the same order of magnitude in patients with and without DM. These observations are similar to those noted in younger patient populations.[13] However, the overall rate of major adverse clinical events was markedly greater than that observed in younger patient populations.[14,15] Only 1 of 10 nonrevascularized 80-year-old patients with DM remained free of any major adverse clinical events during 4 years of follow-up. In contrast, if revascularization was performed, 4 of 10 patients remained free of major adverse clinical events. These numbers point to an urgent need for invasive treatment in elderly patients with DM, particularly because they seem to benefit similarly from revascularization as do patients without DM. For patients with DM, symptom severity and the need for more antianginal drugs was lower after coronary artery bypass graft surgery than after percutaneous coronary intervention. Although this was not a randomized comparison, the results compare favorably with what has been noted as the long-term effects of revascularization in younger patients.[16]

The findings of this study were limited because they were based on a subgroup analysis of the TIME data comparing effectively received invasive versus medical treatment in patients with DM. Although the outcome results were adjusted for clinical variables, and the clinical decision for revascularization was based on symptoms alone, a referral bias for invasive therapy could not be excluded. Furthermore, our results were based on rather small patient numbers. In addition, they did not allow differentiating between the effects of the 2 revascularization methods applied, although the 2 methods were performed on the basis of clinical, angiographic, and feasibility judgments, as is currently done. Thus, these encouraging results for revascularization in elderly diabetic patients need confirmation in larger prospective studies that specifically focus on patients with DM. Until such results are available, one has to rely on findings, such as presented in this report, suggesting that elderly patients with DM should be offered invasive evaluation and revascularization to improve their symptomatic and overall outcomes.

**Acknowledgment:** We gratefully acknowledge the contribution of all participating patients and the work done by all investigators, advisors, and the critical event committee. A list of all investigators has been previously published.[1] We thank Leticia Grize, PhD, Institute of Social and Preventive Medicine, University of Basel, Switzerland, for her statistical support.

1. Trial of invasive versus medical therapy in elderly patients with chronic symptomatic coronary artery disease (TIME). a randomised trial. Lancet 2001;358:951–957.
2. Pfisterer M, Buser P, Osswald S, Allemann U, Amann W, Angehrn W, Eeckhout E, Erne P, Estlinbaum W, Kuster G, et al. Outcome of elderly patients with chronic symptomatic coronary artery disease with an invasive vs optimized medical treatment strategy: one-year results of the randomized TIME trial. *JAMA* 2003;289:1117–1123.
3. Pfisterer M, for the TIME Investigators. Trial of Invasive versus Medical Therapy in the Elderly (TIME): study protocol and patient outline. *Heart Drug* 2001;1:144–147.
4. Bullinger M. German translation and psychometric testing of the SF-36 health survey: preliminary results from the IQOLA project. *Soc Sci Med* 1995;4:1359–1366.
5. Hlatky MA, Boineau RE, Higginbotham MB, Lee KL, Mark DB, Califf RM, Cobb FR, Pryor DB. A brief self-administered questionnaire to determine functional capacity (the Duke Activity Status Index). *Am J Cardiol* 1989;64:651–654.
6. Rose GA. Cardiovascular Survey Methods. 2nd ed. Geneva: WHO, 1982.
7. Pfisterer M. Long-term outcome in elderly patients with chronic angina managed invasively versus by optimized medical therapy: four-year follow-up of the randomized Trial of Invasive versus Medical therapy in Elderly patients (TIME). *Circulation* 2004;110:1213–1218.
8. Stewart AL, Greenfield S, Hays RD, Wells K, Rogers WH, Berry SD, McGlynn EA, Ware JE Jr. Functional status and well-being of patients with chronic conditions. Results from the Medical Outcomes Study. *JAMA* 1989;262:907–913.
9. Sobel BE, Frye R, Detre KM. Burgeoning dilemmas in the management of diabetes and cardiovascular disease: rationale for the Bypass Angioplasty Revascularization Investigation 2 Diabetes (BARI 2D) trial. *Circulation* 2003;107:636–642.
10. Zellweger MJ, Hachamovitch R, Kang X, Hayes SW, Friedman JD, Germano G, Pfisterer ME, Berman DS. Prognostic relevance of symp-

toms versus objective evidence of coronary artery disease in diabetic patients. *Eur Heart J* 2004;25:543–550.
11. Zellweger MJ, Weinbacher M, Zutter AW, Jeger RV, Mueller-Brand J, Kaiser C, Buser PT, Pfisterer ME. Long-term outcome of patients with silent versus symptomatic ischemia six months after percutaneous coronary intervention and stenting. *J Am Coll Cardiol* 2003;42:33–40.
12. Wilson PW, D'Agostino RB, Levy D, Belanger AM, Silbershatz H, Kannel WB. Prediction of coronary heart disease using risk factor categories. *Circulation* 1998;97:1837–1847.
13. Barzilay JI, Kronmal RA, Bittner V, Eaker E, Evans C, Foster ED. Coronary artery disease and coronary artery bypass grafting in diabetic patients aged ≥65 years (report from the Coronary Artery Surgery Study [CASS] Registry). *Am J Cardiol* 1994;74:334–339.
14. Elezi S, Kastrati A, Pache J, Wehinger A, Hadamitzky M, Dirschinger J, Neumann FJ, Schomig A. Diabetes mellitus and the clinical and angiographic outcome after coronary stent placement. *J Am Coll Cardiol* 1998;32:1866–1873.
15. Stein B, Weintraub WS, Gebhart SP, Cohen-Bernstein CL, Grosswald R, Liberman HA, Douglas JS Jr, Morris DC, King SB III. Influence of diabetes mellitus on early and late outcome after percutaneous transluminal coronary angioplasty. *Circulation* 1995; 91:979–989.
16. Bypass Angioplasty Revascularization Investigation (BARI) Group. Influence of diabetes on 5-year mortality and morbidity in a randomized trial comparing CABG and PTCA in patients with multivessel disease. *Circulation* 1997;96:1761–1769.