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Prevalence and impact of a chronic total occlusion in a non-infarct-related artery on long-term mortality in diabetic patients with ST elevation myocardial infarction

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See Editorial, p 1955

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ABSTRACT

Background Recently, a chronic total occlusion (CTO) in a non-infarct-related artery (non-IRA) and not multivessel disease (MVD) alone was identified as an independent predictor of mortality after ST elevation myocardial infarction (STEMI). Patients with diabetes mellitus (DM) constitute a patient group with a high prevalence of MVD and high mortality after STEMI. The prevalence of CTO in a non-IRA was studied and its impact on long-term mortality in STEMI patients with DM was investigated.

Methods Between 1997 and 2007 4506 patients with STEMI were admitted and treated with primary percutaneous coronary intervention (PCI). Patients with DM were identified. The patients were categorised as having single vessel disease (SVD), MVD without CTO and CTO based on the angiogram before PCI.

Results A total of 539 patients (12%) had DM. MVD with or without a CTO was present in 33% of non-diabetic patients and in 51% of diabetic patients. The prevalence of a CTO in a non-IRA was 21% in STEMI patients with DM and 12% in STEMI patients without DM ($p<0.01$). Kaplan–Meier estimates for 5-year mortality in STEMI patients with DM were 25%, 21% and 47% in patients with SVD, MVD without a CTO and MVD with a CTO in a non-IRA, respectively. A CTO in a non-IRA was an independent predictor of 5-year mortality (HR 2.2, 95% CI 1.3 to 3.5, $p<0.01$).

Conclusion The prevalence of a CTO in a non-IRA was increased in STEMI patients with DM. The presence of a CTO in a non-IRA was a strong and independent predictor of 5-year mortality. These results suggest that, particularly in the high-risk subgroup of STEMI patients with DM, MVD has prognostic implications only if a concurrent CTO is present.

INTRODUCTION

Patients with diabetes mellitus (DM) constitute a patient group with a high prevalence of multivessel disease (MVD) and high mortality after ST elevation myocardial infarction (STEMI). Approximately 35–45% of non-diabetic STEMI patients have MVD compared with 60–70% of patients with DM. The higher mortality of STEMI patients with DM has been suggested to be at least partly due to the greater extent of coronary artery disease.^{1–3}

Recently, the presence of a chronic total occlusion (CTO) in a non-infarct-related artery (non-IRA) and not MVD alone was reported to be an independent predictor of mortality after STEMI.^{4–6} Given the greater extent of coronary artery disease in diabetic patients with STEMI, we hypothesised that the prevalence of a CTO in a non-IRA would be higher in this high-risk subgroup. Moreover, the prognostic impact of a CTO in a non-IRA in diabetic patients with STEMI is currently unknown. We therefore studied the prevalence and impact of a concurrent CTO on long-term mortality in STEMI patients with DM.

METHODS

Between 1997 and 2007 a total of 4931 consecutive and unselected patients were admitted to our hospital with STEMI. Acute STEMI was diagnosed when patients had symptoms of an acute myocardial infarction lasting 30 min to 6 h accompanied by an ECG with ST segment elevation >1 mm (0.1 mV) in two or more contiguous leads. Patients were immediately transported to the cardiac catheterisation laboratory and underwent immediate coronary angiography with a view to performing a primary percutaneous coronary intervention (PCI). PCI was performed by standard techniques if the coronary anatomy was suitable. All procedural decisions, including device selection and adjunctive pharmacotherapy such as glycoprotein IIb/IIIa inhibitors, were made at the discretion of the operator. All patients were treated with heparin (5000 IU) and aspirin (900 mg) prior to PCI. If a coronary stent was implanted, ticlopidine or clopidogrel was prescribed according to the guidelines.⁷

Study cohort

Data for the 4931 patients were checked for consistency and completeness. For patients who underwent more than one primary PCI during the study period ($n=147$), only the first intervention was included in this analysis. Patients treated with rescue PCI for failed intravenous thrombolysis ($n=145$), patients without confirmed diagnosis of STEMI ($n=76$) and patients lost to follow-up ($n=57$) were excluded. The remaining 4506 patients constitute the present study cohort. This cohort

has been described previously.⁸ We subsequently identified patients with an established diagnosis of DM at the time of admission from our electronic database for the current analysis.

Definitions

Patients with DM were categorised according to preadmission treatment: either with oral medication or diet-controlled (non-insulin-dependent DM, NIDDM) or with insulin (insulin-dependent DM, IDDM). A CTO was defined as a 100% luminal narrowing in a non-IRA before PCI without antegrade flow or with antegrade or retrograde filling through collateral vessels. MVD was defined as at least one stenosis $\geq 70\%$ in a non-infarct-related epicardial artery or a stenosis $\geq 50\%$ in the left main coronary artery. Shock was defined according to the clinical criteria used in the 'Should we emergently revascularize Occluded Coronaries for cardiogenic shock?' (SHOCK) trial.⁹

Baseline data

All patients undergoing PCI at our institution were prospectively followed. Baseline clinical, angiographic and procedural information was entered by qualified cardiac catheterisation laboratory personnel and interventional cardiologists in a dedicated electronic database.

Follow-up

Information on the vital status was obtained from the institutional follow-up database of patients who underwent PCI. Patients were surveyed 1 year after primary PCI using a mailed self-administered questionnaire. Information on mortality was synchronised with the computerised records from the national population registry (Statistics Netherlands, Voorburg, The Netherlands) and was verified until 1 January 2009. We reviewed the outpatient files and contacted general practitioners by telephone in cases of conflicting or missing data.

Primary outcome

The primary outcome for the present analysis was all-cause 5-year mortality.

Statistical analysis

Statistical analysis was performed with SPSS statistical software Version 17.0 (SPSS Inc). Discrete variables were summarised as frequencies and percentages. Differences in baseline characteristics between the three groups were tested for significance by the χ^2 test. Statistical significance was defined as $p < 0.05$.

Cumulative event rates of all-cause death were estimated using the Kaplan–Meier method. Follow-up for mortality was censored at the date of last follow-up by checking vital status in the Dutch population registry or at 5 years, whichever came first. The log rank statistic was used to test for significant differences in mortality between the groups. HRs for all-cause death were calculated using Cox proportional hazard regression analyses after verification of the proportional hazards assumption. Two multivariate Cox regression models were constructed. We used a categorical variable consisting of three groups to classify patients as having SVD, MVD without CTO or MVD with CTO. The first model included variables for MVD with CTO and MVD without CTO, with SVD as the reference. The second model included variables for MVD with CTO and SVD, with MVD without CTO as the reference. The following covariates were included in both models: age (as a continuous variable, per year increment), male gender, hypertension, smoking, hypercholesterolaemia, previous MI, shock, left anterior descending coronary artery-related MI, post-PCI thrombolysis in

myocardial infarction (TIMI) 3 flow, use of glycoprotein IIb/IIIa inhibitors and stent use. A covariate was allowed in the model if it influenced the model with a likelihood ratio significance level of $p < 0.10$ and removed if its significance level exceeded $p = 0.15$.

RESULTS

Between 1997 and 2007 we treated 4506 patients with STEMI with primary PCI, of whom 539 (12%) had a confirmed diagnosis of DM at admission. Table 1 shows baseline, angiographic and procedural characteristics for the 4506 patients with STEMI with and without DM. Patients with DM were older, more often female and more often had a previous MI and cardiogenic shock at presentation. Furthermore, 51% of patients with DM had MVD compared with 33% of patients without DM ($p < 0.01$). Interestingly, the prevalence of a CTO in a non-IRA was 21% in patients with STEMI with DM compared with 12% in patients with STEMI without DM ($p < 0.01$, figure 1).

Baseline, angiographic and procedural characteristics for the study cohort of 539 patients with DM are shown in table 2. Diabetic patients with MVD (both with and without a CTO) were older, more often had a previous MI and cardiogenic shock at presentation, were more often treated with intra-aortic balloon pump counterpulsation and were less frequently treated with coronary stents and thrombosuction than patients with SVD. Furthermore, patients with a CTO in a non-IRA more often had a previous MI and cardiogenic shock at presentation than those with MVD without a CTO.

Kaplan–Meier estimates of 5-year mortality were 18% in patients with STEMI without DM and 28% in those with DM. Figure 2 shows the Kaplan–Meier estimates of cumulative mortality up to 5 years for non-diabetic and diabetic patients with STEMI with SVD, MVD without a CTO and CTO. In patients with STEMI without DM, mortality increased significantly with increasing severity of coronary artery disease.

Table 1 Baseline characteristics of patients with ST elevation myocardial infarction with and without diabetes mellitus

Baseline characteristics	Patients without diabetes mellitus N = 3967 (88%)	Patients with diabetes mellitus N = 539 (12%)	p Value
Male	73%	63%	<0.01
Age >60 years	49%	66%	<0.01
Hypertension	28%	50%	<0.01
Smoker	45%	32%	<0.01
Hypercholesterolaemia	20%	33%	<0.01
Family history of cardiovascular disease	40%	33%	<0.01
Previous myocardial infarction	12%	23%	<0.01
Shock	7.6%	10%	0.04
Left ventricular ejection fraction <40%*	16%	25%	<0.01
Angiographic characteristics			
LAD-related myocardial infarction	44%	44%	0.86
MVD	33%	51%	<0.01
MVD without CTO	21%	30%	<0.01
MVD with CTO	12%	21%	<0.01
Post-procedural TIMI flow grade 3	88%	87%	0.23
Procedural characteristics			
Thrombosuction performed	32%	25%	<0.01
Intra-aortic balloon pump	8.4%	11%	0.04
Stent placement	75%	69%	<0.01
Glycoprotein IIb/IIIa inhibitor used	26%	26%	1

*Left ventricular ejection fraction was available for 1844/4506 patients. CTO, chronic total occlusion; LAD, left anterior descending coronary artery; MVD, multivessel disease; TIMI, thrombolysis in myocardial infarction.

Figure 1 Prevalence of single vessel disease, multivessel disease without a CTO and CTO in (A) patients with STEMI without diabetes mellitus and (B) patients with STEMI with diabetes mellitus. CTO, chronic total occlusion; MVD, multivessel disease (without CTO); STEMI, ST elevation myocardial infarction; SVD, single vessel disease.

In patients with DM, mortality was significantly higher in patients with a CTO in a non-IRA than in patients with SVD or MVD without a CTO ($p<0.01$), but there was no significant difference in mortality between patients with MVD without a CTO and patients with SVD ($p=0.82$).

Table 3 shows unadjusted and adjusted HRs of significant predictors of 5-year mortality in patients with STEMI with DM. When SVD was used as the reference category, a CTO in a non-IRA was a strong and independent predictor of 5-year mortality (adjusted HR 2.2, 95% CI 1.3 to 3.5, $p<0.01$), whereas MVD without a CTO was not associated with increased 5-year mortality. When MVD without a CTO was used as the reference category, CTO in a non-IRA remained an independent predictor of 5-year mortality (adjusted HR 2.6, 95% CI 1.6 to 4.4, $p<0.01$).

Table 2 Baseline clinical, angiographic and procedural characteristics for 539 patients with ST elevation myocardial infarction with diabetes mellitus

Baseline characteristics	SVD N=264 (49%)	MVD (without CTO) N=162 (30%)	CTO N=113 (21%)	p Value
Male	160 (61)	104 (64)	77 (68)	0.36
Age >60 years	153 (58)	121 (75)	82 (73)	<0.01
Hypertension	137 (52)	83 (51)	53 (47)	0.66
Insulin-dependent diabetes mellitus*	74 (28)	49 (30)	42 (37)	0.21
Smoker	90 (34)	47 (29)	37 (33)	0.55
Hypercholesterolaemia	82 (31)	54 (33)	43 (38)	0.42
Family history of cardiovascular disease	98 (37)	56 (35)	25 (22)	0.02
Previous myocardial infarction	32 (12)	36 (22)	59 (52)	<0.01
Shock	15 (5.7)	16 (9.9)	25 (22)	<0.01
Left ventricular ejection fraction <40%†	23 (22)	17 (28)	11 (31)	0.44
Angiographic characteristics				
LAD-related myocardial infarction	128 (49)	64 (40)	45 (40)	0.12
Post-procedural TIMI flow grade 3	231 (88)	144 (89)	91 (81)	0.11
Procedural characteristics				
Thrombosuction performed	86 (33)	30 (19)	20 (18)	<0.01
Intra-aortic balloon pump	13 (5)	17 (11)	30 (27)	<0.01
Stent placement	196 (74)	106 (65)	71 (63)	0.04
Glycoprotein IIb/IIIa inhibitor used	70 (27)	39 (24)	31 (27)	0.79

Data shown as N (%).

*Compared with non-insulin dependent diabetes mellitus.

†Left ventricular ejection fraction data were available for 202/539 patients.

CTO, chronic total occlusion; LAD, left anterior descending coronary artery; MVD, multivessel disease; SVD, single vessel disease; TIMI, thrombolysis in myocardial infarction.

A 5-year mortality in patients without diabetes mellitus

B 5-year mortality in patients with diabetes mellitus

Figure 2 Kaplan—Meier estimates of 5-year mortality in patients with ST elevation myocardial infarction treated with primary percutaneous coronary intervention. (A) Kaplan—Meier estimates for 5-year mortality in ST elevation myocardial infarction patients without diabetes mellitus. (B) Kaplan—Meier estimates for 5-year mortality in ST elevation myocardial infarction patients with diabetes mellitus. CTO, chronic total occlusion; MVD, multivessel disease (without CTO); SVD, single vessel disease.

DISCUSSION

In this cohort of 4506 patients with STEMI of whom 539 had DM, the prevalence of a CTO in a non-IRA was almost twice as high in diabetic patients as in non-diabetic patients. Moreover, a CTO in a non-IRA was a strong and independent predictor of mortality in patients with STEMI with DM. This is the first study to evaluate the prevalence and prognostic value of a CTO in a non-IRA in diabetic patients with STEMI.

Even with contemporary mechanical reperfusion therapy, mortality after STEMI in patients with DM remains high. Diabetic patients are older, have a higher prevalence of comorbidities and more often have a history of a previous MI.^{1 10 11} Nevertheless, the increased risk associated with DM persists after multivariate adjustment. A number of factors may cause the increased morbidity and mortality after STEMI in diabetic patients. Patients with DM are known to have higher rates of incomplete ST segment resolution and reduced myocardial blush grade after primary PCI for STEMI, suggesting impaired

Table 3 Unadjusted and adjusted significant predictors of 5-year mortality in patients with ST elevation myocardial infarction with diabetes mellitus

	Unadjusted			Adjusted		
	HR	95% CI	p Value	HR	95% CI	p Value
Shock	4.6	3.1 to 6.8	<0.01	3.6	2.4 to 5.6	<0.01
CTO (reference SVD)	3.0	2.0 to 4.6	<0.01	2.2	1.3 to 3.5	<0.01
CTO (reference MVD without CTO)	3.0	1.9 to 4.9	<0.01	2.6	1.6 to 4.4	<0.01
MVD without CTO* (reference SVD)	1.0	0.6 to 1.6	0.99	0.8	0.5 to 1.3	0.42
SVD† (reference MVD without CTO)	1.0	0.6 to 1.6	0.99	1.2	0.7 to 2.0	0.43
Insulin-dependent diabetes mellitus‡	1.4	1.0 to 2.0	0.04	1.8	1.2 to 2.6	0.01
Age (per year increment)	1.03	1.01 to 1.05	<0.01	1.03	1.01 to 2.05	<0.01
Previous myocardial infarction	1.5	1.1 to 2.1	0.02			NS
Smoking	0.7	0.4 to 1.0	0.04			NS
Hypertension	0.6	0.4 to 0.9	<0.01	0.7	0.5 to 0.9	<0.01
Stenting	0.5	0.4 to 0.8	<0.01	0.5	0.3 to 0.7	<0.01
Post-procedural TIMI 3 flow	0.3	0.2 to 0.4	<0.01	0.4	0.3 to 0.7	<0.01

*MVD without CTO was forced into the multivariate model with SVD as the reference.

†SVD was forced into the multivariate model with MVD without CTO as the reference.

‡Compared with non-insulin-dependent diabetes mellitus.

CTO, chronic total occlusion; MVD, multivessel disease; SVD, single vessel disease; TIMI, thrombolysis in myocardial infarction.

reperfusion at the myocardial tissue level.^{12 13} Furthermore, longstanding hyperglycaemia, hyperinsulinaemia and increased circulating free fatty acids induce adverse metabolic changes in the endothelium.^{14 15} DM is also associated with intrinsic myocardial dysfunction, probably as a result of autonomic neuropathy and microvascular dysfunction.^{16 17}

This study confirms and extends previous reports showing that patients with DM have more severe coronary artery disease (ie, a higher prevalence of MVD). Interestingly, we observed that the prevalence of a CTO in a non-IRA was twice as high in patients with STEMI with DM as in patients without DM.

A CTO in a non-IRA has previously been reported to be a predictor of both short- and long-term mortality after STEMI treated with primary PCI.^{4–6} Furthermore, a CTO in a non-IRA was associated with reduced left ventricular ejection fraction (LVEF) during the index hospitalisation and a further reduction in LVEF within the first year thereafter.⁴ We recently showed that mortality in patients with STEMI with cardiogenic shock and MVD is mainly driven by the presence of a CTO in a non-IRA.⁶ Interestingly, in the present study, diabetic patients with MVD without a CTO had a 5-year mortality rate which was comparable to diabetic patients with SVD and comparable to non-diabetic patients with MVD without a CTO. Moreover, in our multivariate Cox regression models the adjusted HR for 5-year mortality of a CTO in a non-IRA was fairly similar when we used SVD as the reference or MVD without CTO as the reference category (2.2 and 2.6, respectively). These results suggest that, particularly in the high-risk subgroup of patients with STEMI with DM, MVD has prognostic implications only if a concurrent CTO is present.

Clinical implications

An aggressive multivessel PCI strategy during and after primary PCI for STEMI has not improved outcome in patients with MVD, both with and without DM. In fact, studies have shown that treatment of non-culprit lesions in patients with STEMI with MVD is associated with a higher post-procedural morbidity rate without a benefit in survival.^{18–20} As in our previous reports, the findings of the present study suggest that additional revascularisation strategies should perhaps be more focused at treating total occlusions rather than stenoses in non-IRAs. Treating a CTO in a non-IRA during the primary procedure does not seem feasible, given the complexity of CTO angioplasty which requires a skilled and experienced operator

and is associated with increased use of contrast medium and longer fluoroscopy time. A staged PCI procedure to revascularise a CTO in a non-IRA after STEMI seems to be a more sensible approach. We have therefore recently initiated the randomised controlled multicentre 'Evaluating XIENCE V and LVF in PCI on occLusiOns afterR STEMI' (EXPLORE) trial to investigate the effects on left ventricular function and remodelling of opening a CTO in a non-IRA in a staged procedure within 1 week after primary PCI.²¹

Study limitations

Several limitations of the current study should be mentioned. The study cohort is comprised of patients with a known diagnosis of DM at admission. We did not routinely measure haemoglobin A_{1c} or test for DM during admission. Furthermore, detailed information on peri- and post-procedural medication (including glucose-regulating medication) was not available. We were therefore not able to assess differences in glycaemic control or adherence to guideline-based post-STEMI therapies. Moreover, we did not routinely store information on pre- or post-PCI renal function in our PCI database. Finally, some overestimation of non-culprit lesions may have occurred as non-culprit lesion stenosis severity was assessed in the acute setting on the infarct angiography by the performing cardiologist.²²

CONCLUSION

Compared with patients with STEMI without DM, the prevalence of a CTO in a non-IRA is increased in patients with STEMI with DM. In patients with DM, 5-year mortality was comparable between patients with SVD and patients with MVD without a CTO. The presence of a CTO in a non-IRA is a strong and independent predictor of 5-year mortality in diabetic patients with STEMI treated with primary PCI. These results suggest that, particularly in the high-risk subgroup of patients with STEMI with DM, MVD has prognostic implications only if a concurrent CTO is present.

Competing interests None.

Contributors BEPMC and LPH contributed equally to this article.

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REFERENCES

1. Mak KH, Moliterno DJ, Granger CB, *et al*. Influence of diabetes mellitus on clinical outcome in the thrombolytic era of acute myocardial infarction. GUSTO-I

- Investigators. Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries. *J Am Coll Cardiol* 1997;**30**:171–9.
2. **van der Schaaf RJ**, Timmer JR, Ottervanger JP, *et al*. Long-term impact of multivessel disease on cause-specific mortality after ST elevation myocardial infarction treated with reperfusion therapy. *Heart* 2006;**92**:1760–3.
3. **van der Schaaf RJ**, Henriques JP, Wiersma JJ, *et al*. Primary percutaneous coronary intervention for patients with acute ST elevation myocardial infarction with and without diabetes mellitus. *Heart* 2006;**92**:117–18.
4. **Claessen BE**, van der Schaaf RJ, Verouden NJ, *et al*. Evaluation of the effect of a concurrent chronic total occlusion on long-term mortality and left ventricular function in patients after primary percutaneous coronary intervention. *JACC Cardiovasc Interv* 2009;**2**:1128–34.
5. **van der Schaaf RJ**, Vis MM, Sjauw KD, *et al*. Impact of multivessel coronary disease on long-term mortality in patients with ST-elevation myocardial infarction is due to the presence of a chronic total occlusion. *Am J Cardiol* 2006;**98**:1165–9.
6. **van der Schaaf RJ**, Claessen BE, Vis MM, *et al*. Effect of multivessel coronary disease with or without concurrent chronic total occlusion on one-year mortality in patients treated with primary percutaneous coronary intervention for cardiogenic shock. *Am J Cardiol* 2010;**105**:955–9.
7. **King SB III**, Smith SC Jr, Hirshfeld JW Jr, *et al*. 2007 focused update of the ACC/AHA/SCAI 2005 guideline update for percutaneous coronary intervention: a report of the American College of Cardiology/American Heart Association Task Force on Practice guidelines. *J Am Coll Cardiol* 2008;**51**:172–209.
8. **Claessen BE**, Kikkert WJ, Engstrom AE, *et al*. Primary percutaneous coronary intervention for ST elevation myocardial infarction in octogenarians: trends and outcomes. *Heart* 2010;**96**:843–7.
9. **Hochman JS**, Sleeper LA, Godfrey E, *et al*. Should we emergently revascularize Occluded Coronaries for cardiogenic shock: an international randomized trial of emergency PTCA/CABG-trial design. The SHOCK Trial Study Group. *Am Heart J* 1999;**137**:313–21.
10. **Franklin K**, Goldberg RJ, Spencer F, *et al*. Implications of diabetes in patients with acute coronary syndromes. The Global Registry of Acute Coronary Events. *Arch Intern Med* 2004;**164**:1457–63.
11. **Jaffe AS**, Spadaro JJ, Schechtman K, *et al*. Increased congestive heart failure after myocardial infarction of modest extent in patients with diabetes mellitus. *Am Heart J* 1984;**108**:31–7.
12. **Prasad A**, Stone GW, Stuckey TD, *et al*. Impact of diabetes mellitus on myocardial perfusion after primary angioplasty in patients with acute myocardial infarction. *J Am Coll Cardiol* 2005;**45**:508–14.
13. **Timmer JR**, van der Horst IC, de Luca G, *et al*. Comparison of myocardial perfusion after successful primary percutaneous coronary intervention in patients with ST-elevation myocardial infarction with versus without diabetes mellitus. *Am J Cardiol* 2005;**95**:1375–7.
14. **Steinberg HO**, Chaker H, Leaming R, *et al*. Obesity/insulin resistance is associated with endothelial dysfunction. implications for the syndrome of insulin resistance. *J Clin Invest* 1996;**97**:2601–10.
15. **Williams SB**, Cosco JA, Roddy MA, *et al*. Impaired nitric oxide-mediated vasodilation in patients with non-insulin-dependent diabetes mellitus. *J Am Coll Cardiol* 1996;**27**:567–74.
16. **Rossen JD**. Abnormal microvascular function in diabetes: relationship to diabetic cardiomyopathy. *Coron Artery Dis* 1996;**7**:133–8.
17. **Scognamiglio R**, Avogaro A, Casara D, *et al*. Myocardial dysfunction and adrenergic cardiac innervation in patients with insulin-dependent diabetes mellitus. *J Am Coll Cardiol* 1998;**31**:404–12.
18. **Corpus RA**, House JA, Marso SP, *et al*. Multivessel percutaneous coronary intervention in patients with multivessel disease and acute myocardial infarction. *Am Heart J* 2004;**148**:493–500.
19. **Chen LY**, Lennon RJ, Grantham JA, *et al*. In-hospital and long-term outcomes of multivessel percutaneous coronary revascularization after acute myocardial infarction. *Am J Cardiol* 2005;**95**:349–54.
20. **Cavender MA**, Milford-Beland S, Roe MT, *et al*. Prevalence, predictors, and in-hospital outcomes of non-infarct artery intervention during primary percutaneous coronary intervention for ST-segment elevation myocardial infarction (from the National Cardiovascular Data Registry). *Am J Cardiol* 2009;**104**:507–13.
21. **van der Schaaf RJ**, Claessen BE, Hoebers LP, *et al*. Rationale and Design of EXPLORE: a Randomized, Prospective, Multicenter Trial Investigating the Impact of Recanalization of a Chronic Total Occlusion on Left Ventricular Function in Patients after Primary Percutaneous Coronary Intervention for Acute ST-Elevation Myocardial Infarction. *Trials* 2010;**11**:89.
22. **Hanratty CG**, Koyama Y, Rasmussen HH, *et al*. Exaggeration of nonculprit stenosis severity during acute myocardial infarction: implications for immediate multivessel revascularization. *J Am Coll Cardiol* 2002;**40**:911–16.