Original Article

# Predictors of Long-term Outcome in Patients with Acute Coronary Syndrome Undergoing Percutaneous Coronary Intervention: A single center registry (THCR)

Seyed Ebrahim Kassaian, MD[1*], Mohammad Sahebjam, MD[1], Mojtaba Salarifar, MD[1], Mohammad Alidoosti, MD[1], Alimohammad Haji Zeinali, MD[1], Davood Kazemi Saleh, MD[2], Hamidreza Poorhoseini, MD[1], Navid Paydari, MD[1], Gholamreza Davoodi, MD[1], Mehran Mahmoodian, MD[1], Seyed Hesameddin Abbasi, MD[1]

[1]*Tehran Heart Center, Tehran University of Medical Sciences, Tehran, Iran.*
[2]*Baghiatallah Hospital, Baghiatallah University of Medical Sciences, Tehran, Iran.*

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## Abstract

***Background:*** *This study sought to access differences in long-term (9 months) outcomes between Acute Coronary Syndrome (ACS) patients who undergo early intervention compared to Percutaneous Coronary Intervention (PCI) in stable and refractory conditions.*

***Methods:*** *Data originated from Tehran Heart Center Registry- interventional cardiology (THCR-IC) and consisted of 1267 patients divided into two categories; 227 patients had features corresponding to acute coronary syndromes (17.9%) and 1040 patients suffered from stable angina (82.1%). They were admitted between April 3, 2003 and April 25, 2004.*

***Results:*** *The clinical success rate of PCI was higher in ACS (97% vs. 94%; P=0.037), while In-hospital complications were similar in both groups. During the follow-up period, clinical restenosis was not significantly different and the overall number of re-interventions caused by restenosis or progression was not more frequent in ACS patients. Also, 1.3% of ACS and 0.4% of SA patients died, but the difference was not statistically significant (P=0.16). Finally, Major Adverse Cardiac Events (MACE) showed no significant difference (5.2% vs. 3.9%; P=0.42). Multivariate analysis showed that female sex (OR=25.6; P=0.003) and previous history of PCI (OR=8.4; P=0.016) were the only strong independent risk factors for major adverse cardiac events. Analyzing ACS patient outcomes using Mantel-Hanzel analysis showed that the female sex was the only factor which strongly increased the incidence of MACE.*

***Conclusion:*** *Both ACS and SA patients who underwent coronary intervention had similar in-hospital and composite major adverse cardiac events, nevertheless female gender must be considered as an independent risk factor for major adverse cardiac events especially in patients with acute coronary syndrome who undergo PCI.*

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***Keywords:*** *Acute coronary syndrome • PCI • Outcome*

## Introduction

Patients with Acute Coronary Syndromes are at risk for adverse cardiac events.1 In a patient with unstable angina, the risk of acute myocardial infarction or death is high: 20% of patients within 30 days after the onset of symptoms and 25% in 6 months.2 Mortality in this group of patients varies from 1.5 to 2.5 after six weeks to 7-10% after a year.3 The

[*]**Corresponding author:** ***Seyed Ebrahim Kassaian,*** *Assistant Professor of Cardiology, Tehran University of Medical Sciences, Tehran Heart Center, North Kargar Street, Tehran, Iran. 1411713138. Tel: +98 21 88029257. Fax: +98 21 88029256. E-mail: ekassaian@yahoo.com.*

general term "Acute Coronary Syndrome" encompasses a wide variety of symptoms in patients with variable history and varying pathophysiological mechanisms.

Since it's inception in 1977, Percutaneous Coronary Intervention (PCI) has become the most common method for coronary revascularization. Randomized trials have demonstrated that patients presenting with an acute coronary syndrome (ACS) who subsequently undergo routine angiography and revascularization, predominantly by PCI, have improved outcomes compared with patients not treated with a routine invasive strategy.4-6

It seems that PCI for ACS patients has been associated with worse procedural, in-hospital and long term outcomes compared PCI under stable angina and elective conditions. A slightly lower success rate and higher peri procedural complication rate has been well documented in literature.7

Despite this fact, PCI especially under protection of platelet glycoprotein (GP) IIb/IIIa receptor inhibitors is a widely adopted treatment strategy for acute coronary syndromes without persistent ST-segment elevation (NSTACS).8

A consequence of PCI, however, is restenosis. There have been reports that restenosis rates with unstable angina are higher than rates with stable angina,9-11 although others demonstrated no difference.12,13 However, the exact relation between restenosis and the effect of timing of PCI in ACS is largely unknown.

It seems to be most important for an interventionist to recognize-as main predictor (the elements that are more effective on individual patient outcome). With this awareness, an operator can decide efficiently about the treatment strategy; whether PCI as an early invasive management is suitable for the operation at hand.

These matters promoted us to perform the present study in Tehran heart center Interventional cardiology registry to assess the short and long-term outcomes and related predictors in acute coronary syndrome (ACS) and to compare those to the outcomes of stable angina patients undergoing PCI with the same conditions.

## Methods

### Design and setting

The present retrospective study was performed in Tehran Heart Center Registry of Interventional cardiology (THCR-IC); that is a single center registry which contains demographic and clinical features plus previous medical antecedents such as risk factors, procedural details and follows up data.

### Study population

During the period April 3, 2003 to April 25, 2004, 1406 patients underwent PCI. 139 patients were excluded due to Primary PCI in the setting of acute ST-elevation MI (n=36), incomplete follow-up (n=103). 1267 patients remained in our study. Of these, 1040 (82.1%) were classified as the stable angina (SA) group and 227 (17.9%) as acute coronary syndrome (ACS) group.

### Definitions

Acute Coronary Syndrome (ACS) is clinically defined as ST-elevation Myocardial Infarction (STEMI), non-ST elevation myocardial Infarction (NSTEMI) and unstable angina of high and low risk types. In the setting of our present study, we selected patients who had the features of ACS within two weeks of PCI.

Unstable angina was defined according to Braunwald classification and described as the sudden appearance and/or worsening of angina, with more frequent and prolonged attacks occurring at rest or on efforts that were previously well tolerated.14 Stable angina was defined according to the Canadian Cardiovascular Society classification (classes 1 through 4); patients displaying effort symptoms according to class I-III were classified as SA group.15

Acute myocardial Infarction (AMI) included patients with a history of NSTEMI in the last two weeks or ST-elevation myocardial infarction from 24 hours to two weeks after the acute event.

### Baseline and clinical characteristics

These characteristics included age, sex, and other demographic data, patients' medical history such as previous history of AMI, previous systemic hypertension, diabetes mellitus and other risk factors. Also, lab data and echocardiographic features as well as the diagnosis of stable or unstable angina pectoris were considered.

### Angiographic and procedural characteristics

Lesion morphology was classified according to the modified American Heart Association/ American Collage of Cardiology (AHA/ACC) classification taskforce.16 Reference vessel diameter, present degree of stenosis and lesion lengths were estimated visually. It was the responsibility of the operators to select the treatment strategy and record selected device, procedural complications and outcome on detailed forms. Stent placement procedures were performed according to standard methods; the size of the balloon and the pressure used during dilation were dependent on the operator's discretion.

### Angioplasty procedure

PCI was carried out with the aid of the standard techniques and pharmacotherapy, as applicable at the time. Routine

preprocedure medication included: ASA 100-325 mg daily and Clopidogrel (Plavix) 600 mg (either 75mg per day for 5 days, 300mg 24 hours before or 600mg 4-6 hours before the procedure), Intravenous Heparin 7500-10000U during procedure and in selected patients, for 12-24 hours following angioplasty. Other medications before, during, as well as after the procedure were administrated according to the clinical situation and concomitant disorders at the discretion of the attending cardiologist.

### *Follow-up*

Follow-up data were obtained from hospital charts through the follow up clinic and supplemented by a structured telephone interview with the patients or one of his or her immediate relatives conducted by an educated general practitioner.

### *Endpoints*

The primary endpoint of this study was In-hospital complications including death, Q or non-Q-wave MI or need for emergency bypass surgery. With due attention to this definition, we descript success rate in our study. Angiographically, success is residual stenosis less than 30% in the target vessel and clinical success is defined as angiographically successful PCI without any severe In-hospital complication. Secondary endpoints consisted of Major Adverse Cardiac events (MACE) including death, non-fatal myocardial infarction and target vessel revascularization (CABG or Repeated PCI in the target vessel).

### *Statistical analysis*

Continuous variables are expressed as mean±SD, and dichotomous variables as frequencies. Categorical variables were compared using the chi-square test and continuous variables by using student t test and p values < 0.05 were considered statistically significant. The impact of different baseline characteristics on outcome was first tested using a simple regression model. Those variables that were significantly associated with any of the measured outcomes were then evaluated with mantel-Hanzel statistics and multiple stepwise regression models using the Cox proportional hazards model. The impact on outcome was expressed as odds ratios with 95% confidence intervals.

## *Results*

The study population consisted of 1267 patients who underwent PCI, of which 227 (17.9%) had the features of acute coronary syndrome and 1040 (82.1%) experienced only stable angina.

Baseline clinical and demographic characteristics of patients have been detailed in Table 1.

Table 1. Baseline clinical and demographic characteristics

| | Acute coronary Syndrome | Stable Angina | P value |
|---|---|---|---|
| **No of cases (%)** | 227(17.9) | 1040(82.1) | |
| **Age** | 58.26±0.71 | 56.97±0.32 | 0.092 |
| **Female Gender** | 78 (34.3) | 293 (28.1) | NS |
| **Clinical characteristics** | | | |
| **Renal insufficiency(Cr>1.5 mg/dl)** | 27 (11.8) | 88 ( 8.4) | NS |
| **MVD** | 75 (33) | 448 (43.07) | NS |
| **EF< 40%** | 44 (0.4) | 150 (14.4) | NS |
| **Positive Family History** | 70 (30.8) | 236 (22.6) | 0.009 |
| **Hyperlipidemia** | 88 (38.7) | 479 (46) | 0.045 |
| **Hypertension** | 93 (40.9) | 320 (30.7) | 0.003 |
| **Diabetes mellitus** | 56 (24.6) | 230 (22.1) | NS |
| **History of smoking** | 81 (35.6) | 376 (36.1) | NS |
| **History of Unstable Angina** | 168 (74) | 253 (24.3) | <0.001 |
| **History of MI** | 106 (46.6) | 356 (34.2) | <0.001 |
| **Prior CABGs** | 9 (3.9) | 30 (2.8) | NS |
| **Prior PCI** | 15 (6.6) | 60 (5.7) | NS |

Categorical variable are expressed as N (%) & continuous variable are expressed as mean±SD
MVD, Multi vessel disease; EF, Left ventricular ejection fraction; CABG, Coronary artery bypass grafting; PCI, Percutaneous coronary intervention

According to this, many/most patients with ACS had a previous experience of myocardial infarction; also more ACS patients had positive family history of CAD and suffered from hypertension. However, hyperlipidemia was significantly more common in SA patients. Furthermore, a larger number of patients with ACS had impaired left ventricular function. Except these findings, the two groups were similar in clinical and demographic characteristics.

### *Angiographic and lesion characteristics*

As demonstrated in table 2, of the 1754 treated lesions, 301 lesions were in ACS and 1453 lesions were in SA patients. According to American Heart Association (AHA/ ACC) classification, lesions with type B2 and C, eccentric and thrombotic lesions were more frequent in ACS patients. Diseased vessel in ACS patients had significantly greater diameter (RVD), while lesion length was often similar in both groups.

Table 2. Angiographic and lesion characteristics

| | Acute Coronary Syndrome | Stable Angina | P value |
|---|---|---|---|
| **No of arteries** | 301(17.1) | 1453(82.9) | |
| **RVD(mm)** | 3.02±0.41 | 2.95±0.40 | 0.006 |
| **Lesion length(mm)** | 15.64±7.07 | 15.42±7.28 | NS |
| **Target territory** | | | |
| **LAD** | 159 (52.8) | 761 (52.3) | NS |
| **LCX** | 61 (20.2) | 339 (23.3) | NS |
| **RCA** | 73 (24.2) | 323 (22.2) | NS |
| **Lesion Characteristics** | | | |
| **Type B2 and C** | 149 (49.5) | 633 (43.5) | 0.004 |
| **Ostial** | 13 (4.3) | 64 (4.4) | NS |
| **Proximal** | 69 (22.9) | 387 (26.6) | NS |
| **Long (11-20mm)** | 135 (44) | 693 (47) | NS |
| **Diffuse (>20mm)** | 40 (13.2) | 199 (13.6) | NS |
| **Calcification** | 5 (1.6) | 15 (1.0) | NS |
| **Bifurcation** | 23 (7.6) | 109 (7.5) | NS |
| **Eccentric** | 73 (24.2) | 278 (19.1) | 0.043 |
| **Thrombus** | 17 (5.6) | 25 (1.7) | <0.001 |
| **Total occlusion** | 29 (9.6) | 143 (9.8) | NS |

Categorical variable are expressed as N (%) & continuous variable are expressed as mean±SD
RVD, Reference vessel diameter; LAD, Left anterior descending artery; LCX, Left circumflex artery; RCA, Right coronary artery

### *Procedural and early outcomes*

As detailed in table 3, length and diameter of stents used in ACS patients compared with stable angina patients were significantly higher. Also, the percent of preprocedural stenosis was higher in ACS while SA patients had more residual stenosis. The clinical success rate of PCI was higher in ACS while In-hospital complications were similar in both groups.

Table 3. Procedural variables

| | Acute Coronary Syndrome | Stable Angina | P value |
|---|---|---|---|
| **Preprocedural stenosis (%)** | 91.38±8.6 | 88.1±10.2 | <0.001 |
| **Post procedural stenosis (%)** | 2.90±0.70 | 5.54±0.45 | 0.015 |
| **Stent diameter (mm)** | 3.06±0.37 | 3.00±0.36 | 0.015 |
| **Stent length (mm)** | 16.98±5.57 | 16.11±5.36 | 0.018 |
| **Success rate** | 292 (97) | 1366 (94) | 0.037 |
| **In-hospital complications** | 22 (7.3) | 79 (5.43) | NS |

Categorical variable are expressed as N (%) & continuous variable are expressed as mean±SD

### *Following up and late outcomes*

Follow up data (table 4) were available in 1130 (89%) patients from among the 1267 studied (92% of ACS and 88% of SA patients). Follow up duration was slightly more in SA patients which does not seem to be clinically significant (8.9±2.3 months in SA and 8.5±2.4 in ACS). Clinical restenosis was not significantly different in the two groups and the overall number of re-interventions caused by restenosis or progression, as well as the repeat PCI or CABG was not more frequent in ACS patients. During the follow up, 1.3% of ACS and 0.4% of SA patients died, but the difference was not statistically significant (P=0.16). MACE showed no significant difference (5.2% vs. 3.9%) during the follow-up period.

Table 4. Follow-up data

| | Acute Coronary Syndrome | Stable Angina | P value |
|---|---|---|---|
| **Follow up duration (m)** | 8.52±2.45 | 8.95±2.31 | 0.019 |
| **Nonfatal MI** | 0 | 7 (0.6) | NS |
| **TVR** | 9 (3.9) | 31 (2.9) | NS |
| **CABG** | 6 (0.4) | 14 (1.3) | NS |
| **Repeated PCI** | 3 (1.3) | 20 (1.9) | NS |
| **TLR** | 3 (1.3) | 12 (1.1) | NS |
| **Death** | 3 (1.3) | 5 (0.4) | NS |
| **Any MACE** | 12 (5.2) | 41 (3.9) | NS |

Categorical variable are expressed as N (%) & continuous variable are expressed as mean±SD
MI, myocardial infarction; TVR, Target vessel restenosis; TLR, Target lesion restenosis; CABG, Coronary artery bypass grafting; PCI, Percutaneous coronary intervention; MACE, Major adverse cardiac events

The repeat PCI or CABG was not more frequent in ACS patients. During the follow up, 1.3% of ACS and 0.4% of SA patients died, but the difference was not statistically significant (P=0.16). The Major Adverse Cardiac Events (MACE) showed no significant difference (5.2% vs. 3.9%) during the follow-up period.

### *Multivariate analysis*

In view of the fact that differences were encountered in baseline, lesion and procedural characteristics, which might confound the long term outcomes especially the major adverse cardiac events, the Mantel-Hanzel and multivariate logistic stepwise regression analysis was carried out. After considering all factors which might have an effect in MACE, we found that female sex (OR=25.6; P=0.003) and previous history of PCI (OR=8.4; P=0.016) were the only strong

independent risk factors for major adverse cardiac events. Additional statistical analysis with Mantel-Hanzel method showed that the female sex was the only factor which strongly increased the incidence of MACE. It must be considered that female gender frequency and prevalence of previous PCI were not different between the two groups.

## Discussion

PCI is an attractive therapeutic option in ACS that is fraught with risk not seen in patients with stable angina. Injured, 'unstable' plaque, intraluminal white, platelet-rich thrombus, systemic coagulation and fibrinolytic disturbances create a very specific situation. Thus, lower clinical success and higher complication rates in ACS patients undergoing PCI is not unexpected.7,17 Unlike some studies, the present study demonstrated higher clinical success and similar in-hospital complication rates in ACS patients.

Surprisingly, we found no difference concerning early outcome in ACS compared to SA patients. A higher incidence of restenosis after PCI in patients with ACS was described by many investigators, but not all.18-20 In our experience, clinical restenosis rate (TLR and TVR) is not significantly more frequent in ACS patients. Also, the present study showed no difference in other long-term outcomes such as need for revascularization, death and composite of major adverse cardiac events between ACS and SA patients, while according to some studies acute coronary syndrome is an independent risk factor for worse outcome of PCI.

However, the optimal timing of PCI in these patients remains uncertain. The question remains: to what extent should the patient be stabilized before the procedure? Recent guidelines suggest a relatively early intervention, especially in high risk patients with ACS,14,15 after various reports demonstrated a reduction in myocardial infarction (MI) and possibly death for invasively treated versus conservatively treated patients.13,16

In five large, randomized trials (Veterna affairs Non-Q-wave Infarction strategy in hospital (VANQWISH]),18 Fragmin and Fast revascularization during instability in coronary artery disease(FRISC II),6 Treat Angina with an Invasive or Conservative Strategy-Thrombolysis in Myocardial Infarction 18 (TACTICS-TIMI 18),16 TIMI IIIB,19 and the third randomized Intervention treatment of Angina (RITA-3)20 a routine, early invasive strategy (early angiography followed by revascularization, depending on angiographic findings) was compared with a "Conservative" strategy (angiography and subsequent revascularization only if medical therapy failed or substantial residual ischemia was documented). An early invasive strategy was shown to be beneficial in the FRISCII, TACTICS-TIMI 18, and RITA-3 studies, especially in the subgroup of high risk patients, such as those presenting with an elevated cardiac Troponin level.

As may be concluded from the earlier reports, result of PCI is better in stabilized angina than in refractory ones.9,21,22 In VANQWISH trial,18 early invasive therapy brought even worse results than the initially conservative strategy. Numerous objections have been put forward with respect to this trial. Nevertheless, some recent studies have clearly proven the superiority of the early invasive strategy over the more conservative approach.

RITA-3 randomized trial concluded that in patients presenting with unstable coronary artery disease, an interventional strategy is preferable to a conservative strategy, mainly because of the significant reduction in refractory or severe angina, and with no increased risk of death or myocardial infarction. FRISCII and TACTICS-TIMI18 have demonstrated similar results. According to these studies, in ACS, the early invasive approach leads to a sustained reduction in mortality, cardiac morbidity, need for repeat hospital admissions and late revascularization procedures. The latest ICTUS trial23 study concluded that either optimized medical therapy and selective invasive strategy or early invasive strategy in an ACS without ST-segment elevation leads to similar results and did not show superiority for either one of them. These could be inferred from the recent investigations in the stent era, the low-molecular-weight heparin and aggressive antiplatelet therapy, including IIb/IIIa receptor inhibitors. The initial 'cooling off' therapy improves the results of coronary interventions.24-27

Several factors may confound our results about long-term outcomes of ACS patients, predominantly the differences in baseline, lesion and procedural characteristics. Logistic stepwise regression analysis clearly showed that female gender and history of prior PCI were independent risk factors for major adverse cardiac events; also Mantel-Hanzel analysis demonstrated that female gender must be considered an important predictor of major adverse cardiac events in ACS patients. In a prospective study,28 it was demonstrated that women treated with very early aggressive revascularization with coronary stenting of and

culprit lesion as the primary revascularization strategy had a better long-term outcome as compared with men. Female gender independently reduced the risk of death or MI like results derived from TACTICS-TIMI1816 study, whereas subgroup analysis in FRISCII study29 showed a worse in-hospital and long-term outcome in women compared with men who were treated similarly, confirmed by our findings in the present study.

The association between a prior PCI and outcome following PCI in ACS has not been previously examined in detail. In a pooled analysis of three randomized ACS trials (GUSTOIIB, PURSUIT, and PARAGONE-B),30 it was concluded that patients with prior PCI had a lower mortality rate compared with patients without prior PCI. Furthermore, patients with prior PCI had a higher incidence of MI compared with patients without prior PCI, however no difference was observed in the composite of death or myocardial infarction between these

patients. Another study showed a significantly lower event-free survival at 9-month follow up despite similar in-hospital complication in patients with prior PCI.31

## Conclusion

Although both ACS and SA patients treated with aggressive revascularization with coronary intervention had similar in-hospital and composite of major adverse cardiac events as a long-term outcome, female gender must be considered as an independent risk factor for major adverse cardiac events in patients with ACS who undergo PCI.

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## References

1. Hamm CW, Braunwald E. A classification of unstable angina revisited. Circulation 2000;102:118-122.
2. Klootwijk P, Hamm C. Acute coronary syndromes: diagnosis. Lancet 1999;354:867-869.
3. Theroux P, Fuster V. Acute coronary syndromes. Unstable angina and non-Q-wave myocardial infarction. Circulation 1998;7:1195–1206.
4. Cannon CP, Weintraub WS, Demopoulos LA. Comparison of early invasive and conservative strategies in patients with unstable coronary syndromes treated with the glycoprotein IIb/IIIa inhibitor tirofiban. N Engl J Med 2001;344:1879–1887.
5. Lagerqvist B, Husted S, Kontny F. A long-term perspective on the protective effects of an early invasive strategy in unstable coronary artery disease: two-year follow-up of the FRISC-II invasive study. J Am Coll Cardiol 2002;40:1902–1914.
6. FRagmin and Fast Revascularisation during InStability in Coronary artery disease Investigators. Invasive compared with non-invasive treatment in unstable coronary-artery disease: FRISC II prospective randomised multicentre study. Lancet 1999;354:708–715.
7. Piana RN, Ahmed WH, Chaitman B. Effect of transient abrupt vessel closure during otherwise successful angioplasty for unstable angina on clinical outcome at six months. J Am Coll Cardiol 1999;33:73-78.
8. Ronner E, Boersma E, Laarman G.J. Early Angioplasty in Acute Coronary Syndromes without Persistent ST-Segment Elevation Improves Outcome But Increases the Need for Six-Month Repeat Revascularization An Analysis of the PURSUIT Trial. J Am Coll Cardiol 2002;39:1924-1929.
9. Feyter PJ, Suryapranata H, Serruys PW. Coronary angioplasty for unstable angina: immediate and late results in 200 consecutive patients with identification of risk factors for unfavorable early and late outcomes. J Am Coll Cardiol 1988;12:324–333.
10. Hermans WR, Foley DP, Rensing BJ. The Multicenter European Research Trial with Cilazapril after Angioplasty to prevent Transluminal Coronary Obstruction and Restenosis (MERCATOR) Study Group. Morphologic changes during follow-up after successful percutaneous transluminal coronary balloon angioplasty: quantitative angiographic analysis in 778 lesions—further evidence for the restenosis paradox. Am Heart J 1994;127:483–94.
11. The PURSUIT Trial Investigators. Inhibition of platelet glycoprotein IIb/IIIa with eptifibatide in patients with acute coronary syndromes. N Engl J Med 1998;339:436–443.
12. Mintz GS, Popma JJ, Pichard AD. Intravascular ultrasound predictors of restenosis after percutaneous transcatheter coronary revascularization. J Am Coll Cardiol 1996; 27:1678–1687.
13. Keelan ET, Nunez BD, Grill DE. Comparison of immediate and long-term outcomes of
coronary angioplasty performed for unstable angina and rest pain in men and women. Mayo Clin Proc 1997;72:5–12.
14. Stone GW, Grines CL, Browne KF. Comparison of in-hospital outcome in men versus women treated by either thrombolytic therapy or primary coronary angioplasty for acute myocardial infarction. Am J Cardiol 1995;75:987–992.
15. Weaver WD, White HD, Wilcox RG. Comparisons of characteristics and outcomes among women and men with acute myocardial infarction treated with thrombolytic therapy. JAMA 1996;275:777–782.
16. Cannon CP, Weintraub WS, Demopoulos LA. Comparison of early invasive and conservative strategies in patients with unstable coronary syndromes treated with the glycoprotein IIb/IIIa receptor inhibitor tirofiban. N Engl J Med 2001;334:1879–1887.
17. Wallentin L, Lagerqvist B, Husted S. Outcome at 1 year after an invasive compared with a non-invasive strategy in unstable coronary-artery disease: the Fast Revascularisation during Instability in Coronary artery disease (FRISC II) invasive randomized trial. Lancet 2000;356:9–16.
18. Boden WE, O'Rourke RA, Crawford MH. Outcomes in patients with acute non-Q-wave myocardial infarction randomly assigned to an invasive as compared with a conservative management strategy. N Engl J Med 1998;338:1785-1792.
19. The TIMI IIIB Investigators. Effects of tissue plasminogen activator and a comparison of early invasive and conservative strategies in unstable angina and non-Q-wave myocardial infarction: results of the TIMI IIIB trial. Circulation 1994;89:1545-1556.
20. Fox KA, Poole-Wilson PA, Henderson RA. Interventional versus conservative treatment for patients with unstable angina or non-ST-elevation myocardial infarction: the British Heart Foundation RITA 3 randomised trial. Lancet 2002;360:743-751.
21. Plokker HWT, Ernst SMPG, Bal ET. Percutaneous transluminal coronary angioplasty in patients with unstable angina pectoris refractory to medical therapy: long term clinical and angiographic results. Cathet Cardiovasc Diagn 1988;14:5-8.
22. Morrison DA, Sacks J, Grover F, Hammermeister KE. Effectiveness of percutaneous transluminal coronary angioplasty for patients with medically refractory angina pectoris and high risk of adverse outcomes with coronary artery bypass grafting. Am J Cardiol 1995;75:237-470.
23. Robbert JDW, Windhausen F, Hein Cornel J. Early Invasive versus Selectively Invasive Management for Acute Coronary Syndromes, N Engl J Med 2005;353:1095-1104.
24. Fox KAA. Comparing trials of glycoprotein IIb/IIIa receptor antagonists. Eur Heart J 1999;1(suppl R): 10-17.

25. Boersma E, Akkerhuis K.M, Theroux P. Platelet glycoprotein IIb/IIIa receptor inhibition in non-ST-elevation acute coronary syndrome. Early benefit during medical treatment only, with additional protection during percutaneous coronary intervention. Circulation 1999;100:2045-2048.
26. Harrington RA, Simoons ML. What have we learned from the recent large trials in acute coronary syndromes without ST-segment elevation? Eur Heart J 2000;21:702-704.
27. Purcell H, Fox K.M. Improving outcome in acute coronary syndromes — as good as it gets? Eur Heart 1999;20:1533-1537.
28. Mueller C, Neumann F.J, Roskamm H. Women Do Have an Improved Long-Term Outcome After Non–ST-Elevation Acute Coronary Syndromes Treated Very Early and Predominantly With Percutaneous Coronary Intervention. J Am Coll Cardiol 2002;40:245-250.
29. Lagerqvist B, Safstrom K, Stahle E. Is early invasive treatment of unstable coronary artery disease equally effective for both women and men? J Am Coll Cardiol 2001;38:41–8.
30. Labinaz M, Mathias J, Pieper K. Outcomes of patients with acute coronary syndromes and prior percutaneous coronary intervention: a pooled analysis of three randomized clinical trials. Eur Heart J 2005;26:128-136.
31. Arjomand H, Willerson JT, Homes DR, Bamlet WR, Surabhi SK. Outcome of patients with prior percutaneous revascularization undergoing repeat coronary intervention (from the PRESTO trial). Am J Cardiol 2005;96:741-746.