

Clinical trials of myocardial revascularization for acute coronary syndrome in all type of patients

TrialResults-center www.trialresultscenter.org

1 cooling-off strategy

| Trial | Treatments | Patients | Trials design and methods |
|---|---|---|------------------------------------|
| early intervention vs early strategy | | | |
| ISAR-COOL , 2003 n=207/203 follow-up: 1 mo | Prolonged (3 to 5 days) antithrombotic pretreatment (Cooling-Off strategy) before intervention versus early intervention after pretreatment for less than 6 hours | patients with symptoms of unstable angina plus either ST-segment depression or elevation of cardiac troponin T levels | Parallel groups open Germany |

References

ISAR-COOL, 2003:

Neumann FJ, Kastrati A, Pogatsa-Murray G, Mehilli J, Bollwein H, Bestehorn HP, Schmitt C, Seyfarth M, Dirschinger J, Schmig A Evaluation of prolonged antithrombotic pretreatment ("cooling-off" strategy) before intervention in patients with unstable coronary syndromes: a randomized controlled trial. JAMA 2003;290:1593-9 [[14506118](#)]

2 early invasive strategy

| Trial | Treatments | Patients | Trials design and methods |
|---|---|---|--|
| routine invasive strategy vs conservervative strategy | | | |
| ICTUS , 2007 [ISRCTN82153174] n=604/596 follow-up: 12 mo (4y) | early invasive strategy versus selective invasive treatment strategy | patients with nonST-segment elevation acute coronary syndrome and elevated cardiac troponin T | Parallel groups open Netherlands |
| FRISC 2 , 1999 n=1222/1234 follow-up: 24 mo | early invasive treatment strategy: angiography within 7 days aiming for revascularisation versus non-invasive treatment strategy: angiography only in patients with refractory or recurrent symptoms despite maximum medical treatment or severe ischemia during exercise test before discharge | patients with nonST-segment elevation acute coronary syndrome | Factorial plan Open Scandinavia |

continued...

| Trial | Treatments | Patients | Trials design and methods |
|---|---|--|---|
| NQWMI (Eisenberg) , 2005 n=42/46 follow-up: 12 months | Invasive (angiography at days 2 to 5) versus Noninvasive (stress testing at day 2 to 5) | patients with nonQ-wave myocardial infarction | Parallel groups open Canada |
| RITA 3 , 2002 [ISRCTN07752711r] n=895/915 follow-up: 24 mo (60 mo) | routine angiography followed by revascularisation/pj versus conservative strategy (ischaemia-driven or symptom-driven angiographyS | patients with nonST-segment elevation acute coronary syndrome | Parallel groups open UK |
| TACTICS-TIMI 18 , 2001 n=1114/1106 follow-up: 6 mo | early invasive management strategy versus conservative management strategy | patients with nonST-segment elevation acute coronary syndrome | Parallel groups open 9 countries |
| TRUCS , 2000 n=76/72 follow-up: 12 mo | invasive strategy versus conservative strategy | patients with nonST-segment elevation acute coronary syndrome in geographically isolated hospitals without cardiac surgical facilities | Parallel groups Greece |
| VINO , 2002 n=64/67 follow-up: 6 mo | first day angiography / angioplasty strategy versus early conservative therapy | patients with nonST-segment elevation acute coronary syndrome | Parallel groups open Czech Republic |
| the Italian Elderly ACS study ongoing [NCT00510185] n=NA follow-up: | early aggressive approach versus initially conservative approach | patients older than 74 years of age with NSTEACS | |
| routine invasive strategy - noncomtemporary vs concervative strategy | | | |
| MATE , 1998 n=111/90 follow-up: 21 mo | early triage angiography and subsequent therapies based on the angiogram versus conventional medical therapy | acute MI ineligible for thrombolytic therapy within 24 h of symptoms | Parallel groups open US |
| TIMI 3B (PTCA) , 1994 n=740/733 follow-up: 12 mo | Early invasive strategy: systematic angiography (18-48h after randomisation) and revascularisation (PTCA or CABG) versus Early elective strategy: angiography and revascularisation only in case of ischemic recurrence (see paper) | patient with unstable angina or non Q wave MI within 24hrs of onset | Factorial plan Open USA & Canada |
| VANQWISH , 1998 n=462/458 follow-up: 23 mo | invasive management versus conservative management: medical therapy with subsequent invasive management if indicated by the development of spontaneous or indicible ischemia within 24-72 hours | Patients with NonQ-wave myocardial infarction | Parallel groups Open US |
| early invasive management vs delayed invasive strategy | | | |

continued...

| Trial | Treatments | Patients | Trials design and methods |
|---|---|---|--|
| TIMACS , 2009 [NCT00552513] n=1593/1438 follow-up: 6 months | early invasive management: angiography within 24 hours followed by PCI or CABG as appropriate versus delayed invasive strategy: angiography after 36 hours followed by PCI or CABG as appropriate | patients with unstable angina or non-ST-segment-elevation MI (NSTEMI) | Parallel groups open 30 countries |
| immediate invasive management vs delayed invasive strategy | | | |
| OPTIMA , 2009 [ISRCTN80874637] n=73/69 follow-up: 30 days | immediate angioplasty under triple antiplatelet therapy protection versus deferred angioplasty | patients with non-ST-segment elevation acute coronary syndromes eligible for percutaneous coronary intervention | Parallel groups open The Netherland, England |
| ABOARD , 2009 [NCT00442949] n=175/177 follow-up: 1 month | immediate catheterization and revascularization versus catheterization and revascularization on the next working day (between 8 and 60 hours after enrollment) | patient with non ST-elevation acute coronary syndrome | Parallel groups open France |

References

ICTUS, 2007:

Hirsch A, Windhausen F, Tijssen JG, Verheugt FW, Cornel JH, de Winter RJ Long-term outcome after an early invasive versus selective invasive treatment strategy in patients with non-ST-elevation acute coronary syndrome and elevated cardiac troponin T (the ICTUS trial): a follow-up study. *Lancet* 2007;369:827-35 [[17350451](#)]

de Winter RJ, Windhausen F, Cornel JH, Dunselman PH, Janus CL, Bendermacher PE, Michels HR, Sanders GT, Tijssen JG, Verheugt FW Early invasive versus selectively invasive management for acute coronary syndromes. *N Engl J Med* 2005;353:1095-104 [[16162880](#)]

FRISC 2, 1999:

Invasive compared with non-invasive treatment in unstable coronary-artery disease: FRISC II prospective randomised multicentre study. FRagmin and Fast Revascularisation during InStability in Coronary artery disease Investigators. *Lancet* 1999;354:708-15 [[10475181](#)]

Lagerqvist B, Husted S, Kontny F, Stahle E, Swahn E, Wallentin L 5-year outcomes in the FRISC-II randomised trial of an invasive versus a non-invasive strategy in non-ST-elevation acute coronary syndrome: a follow-up study. *Lancet* 2006;368:998-1004 [[16980115](#)]

Lagerqvist B, Husted S, Kontny F, Nslund U, Sthle E, Swahn E, Wallentin L 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;40:1902-14 [[12475448](#)]

Lagerqvist B, Husted S, Kontny F, Sthle E, Swahn E, Wallentin L 5-year outcomes in the FRISC-II randomised trial of an invasive versus a non-invasive strategy in non-ST-elevation acute coronary syndrome: a follow-up study. *Lancet* 2006 Sep 16;368:998-1004 [[16980115](#)]

NQWMI (Eisenberg), 2005:

Eisenberg MJ, Teng FF, Chaudhry MR, Ortiz J, Sobkowski W, Ebrahim I, Saligrama RS, Serio K, Lader E, Pilote L Impact of invasive management versus noninvasive management on functional status and quality of life following non-Q-wave myocardial infarction: a randomized clinical trial. *Am Heart J* 2005;149:813-9 [[15894961](#)]

RITA 3, 2002:

Fox KA, Poole-Wilson PA, Henderson RA, Clayton TC, Chamberlain DA, Shaw TR, Wheatley DJ, Pocock SJ Interventional versus conservative treatment for patients with unstable angina or non-ST-elevation myocardial infarction: the British Heart Foundation RITA 3 randomised trial. *Randomized Intervention Trial of unstable Angina. Lancet* 2002 Sep 7;360:743-51 [[12241831](#)]

Fox KA, Poole-Wilson P, Clayton TC, Henderson RA, Shaw TR, Wheatley DJ, Knight R, Pocock SJ 5-year outcome of an interventional strategy in non-ST-elevation acute coronary syndrome: the British Heart Foundation RITA 3 randomised trial. *Lancet* 2005;366:914-20 [[16154018](#)]

TACTICS-TIMI 18, 2001:

Cannon CP, Weintraub WS, Demopoulos LA, Vicari R, Frey MJ, Lakkis N, Neumann FJ, Robertson DH, DeLucca PT, DiBattiste PM, Gibson CM, Braunwald E 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 Jun 21;344:1879-87 [[11419424](#)]

TRUCS, 2000:

Michalis LK, Stroumbis CS, Pappas K, Sourla E, Niokou D, Goudevenos JA, Siogas C, Sideris DA Treatment of refractory unstable angina in geographically isolated areas without cardiac surgery. Invasive versus conservative strategy (TRUCS study). *Eur Heart J* 2000;21:1954-9 [[11071801](#)]

VINO, 2002:

Spacek R, Widimsky P, Straka Z, Jiresova E, Dvorak J, Polasek R, Karel I, Jirmar R, Lisa L, Budesinsky T, Malek F, Stanka P Value of first day angiography/angioplasty in evolving Non-ST segment elevation myocardial infarction: an open multicenter randomized trial. The VINO Study. *Eur Heart J* 2002 Feb;23:230-8 [[11792138](#)]

the Italian Elderly ACS study, 0:

Savonitto S, De Servi S, Petronio AS, Bolognese L, Cavallini C, Greco C, Indolfi C, Visconti LO, Piscione F, Ambrosio G, Galvani M, Marzocchi A, Santilli I, Steffenino G, Maseri A Early aggressive vs. initially conservative treatment in elderly patients with non-ST-elevation acute coronary syndrome: the Italian Elderly ACS study. *J Cardiovasc Med (Hagerstown)* 2008;9:217-26 [[18301136](#)]

MATE, 1998:

McCullough PA, O'Neill WW, Graham M, Stomel RJ, Rogers F, David S, Farhat A, Kazlauskaitė R, Al-Zagoum M, Grines CL A prospective randomized trial of triage angiography in acute coronary syndromes ineligible for thrombolytic therapy. Results of the medicine versus angiography in thrombolytic exclusion (MATE) trial. *J Am Coll Cardiol* 1998 Sep;32:596-605 [[9741499](#)]

TIMI 3B (PTCA), 1994:

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. Thrombolysis in Myocardial Ischemia. *Circulation* 1994;89:1545-56 [[8149520](#)]

VANQWISH, 1998:

Boden WE, O'Rourke RA, Crawford MH, Blaustein AS, Deedwania PC, Zoble RG, Wexler LF, Kleiger RE, Pepine CJ, Ferry DR, Chow BK, Lavori PW Outcomes in patients with acute non-Q-wave myocardial infarction randomly assigned to an invasive as compared with a conservative management strategy. Veterans Affairs Non-Q-Wave Infarction Strategies in Hospital (VANQWISH) Trial Investigators. *N Engl J Med* 1998;338:1785-92 [[9632444](#)]

TIMACS, 2009:

Mehta SR et al. Randomized comparison of early vs delayed invasive strategies in high risk patients with non-ST-segment elevation acute coronary syndromes: Main results of the Timing of Intervention in Acute Coronary Syndromes (TIMACS) trial American Heart Association 2008 Scientific Sessions; November 10, 2008; New Orleans, LA. Late Breaking Clinical Trials Session 2

Mehta SR, Granger CB, Boden WE, Steg PG, Bassand JP, Faxon DP, Afzal R, Chrolavicius S, Jolly SS, Widimsky P, Avezum A, Rupprecht HJ, Zhu J, Col J, Natarajan MK, Horsman C, Fox KA, Yusuf S Early versus delayed invasive intervention in acute coronary syndromes. *N Engl J Med* 2009 May 21;360:2165-75 [[19458363](#)]

OPTIMA, 2009:

Riezebos RK, Ronner E, Ter Bals E, Slagboom T, Smits PC, ten Berg JM, Kiemeneij F, Amoroso G, Patterson MS, Suttorp MJ, Tijssen JG, Laarman GJ Immediate versus deferred coronary angioplasty in non-ST-segment elevation acute coronary syndromes. *Heart* 2009 May;95:807-12 [[19098058](#)]

ABOARD, 2009:

Montalescot G, Cayla G, Collet JP, Elhadad S, Beygui F, Le Breton H, Choussat R, Leclercq F, Silvain J, Duclos F, Aout M, Dubois-Rand JL, Barthlmy O, Ducrocq G, Bellemain-Appaix A, Payot L, Steg PG, Henry P, Spaulding C, Vicaut E Immediate vs delayed intervention for acute coronary syndromes: a randomized clinical trial. *JAMA* 2009 Sep 2;302:947-54 [[19724041](#)] [10.1001/jama.2009.1267](#)

3 fibrinolytic

| Trial | Treatments | Patients | Trials design and methods |
|--|---|---|--|
| anistreplase vs placebo | | | |
| UNASEM , 1992 n=80/79 follow-up: hospital stay, 1y | anistreplase IV 30 UI over 5 minutes versus placebo | Patients without a previous myocardial infarction, with a typical history of unstable angina and ECG abnormalities indicative of ischemia | Parallel groups double blind Europe |
| intracoronary urokinase vs placebo | | | |
| TAUSA , 1994 n=232/237 follow-up: hospital stay | intracoronary urokinase 250000 UI or 500000 UI versus placebo | ischemic rest pain with or without a recent (<1 month) infarction | Parallel groups double blind USA |
| t-PA vs placebo | | | |
| Topol , 1988 n=20/20 follow-up: hospital stay | intravenous tissue plasminogen activator (t-PA) versus placebo | patients with angina at rest and provokable ischemia (pacing induced) | Parallel groups open USA |
| TIMI 3A , 1993 n=150/156 follow-up: hospital stay | 90-minute front-loaded infusion of t-PA (0.8 mg/kg i.v.; maximum, 80 mg) versus placebo | patients with unstable angina or non-Q wave myocardial infarction | Parallel groups double blind USA, canada |
| Nicklas , 1989 n=20/20 follow-up: | rt-PA, 150 mg/8 h versus placebo | patients with rest angina, angiographically documented coronary artery disease and pacing-induced ischemia | Parallel groups Double blind USA |
| Gold , 1987 n=12/12 follow-up: | intravenous recombinant human tissue-type plasminogen activator (rt-PA). versus placebo | chest pain at rest with transient ST segment deviation of at least 1 mm | Parallel groups |
| Williams , 1990 n=45/22 follow-up: | tissue-type plasminogen activator (rt-PA) (0.75 mg/kg over 1 hour or (0.75 mg/kg over 1 hour; total dose, 100 mg over 6 hours) versus placebo | rest angina and angiographic evidence of coronary stenosis | Parallel groups double blind USA |
| Freeman , 1992 n=35/35 follow-up: in hospital | tissue-type plasminogen activator (t-PA) (0.49 MU/kg for 1 hour followed by 0.07 MU/kg per hour for 9 hours) versus placebo | patients with unstable angina | Parallel groups double blind USA |
| van der Brand , 1991 n=19/17 follow-up: hospital stay | alteplase 100 mg in 3 h versus placebo | patients with angina at rest, despite bedrest and medical treatment | Parallel groups double blind The Netherlands |
| charbonnier , 1992 n=25/25 follow-up: | rt-PA 100 mg/90 minutes (10 mg bolus + 90 mg/90 minutes) versus placebo | unstable angina pectoris | Parallel groups double blind |

continued...

| Trial | Treatments | Patients | Trials design and methods |
|--|--|--|--|
| Ardissino , 1990 n=12/12 follow-up: in hospital | recombinant tissue-type plasminogen activator (rt-PA) followed by heparin versus heparin alone | unstable angina refractory to conventional medical treatment | Parallel groups double blind Italy |
| TIMI 3B , 1995 n=729/744 follow-up: 1 year | tissue-type plasminogen activator (t-PA) versus placebo | patients with unstable angina and non-Q wave myocardial infarction | Factorial plan Double blind |

References

UNASEM, 1992:

Br FW, Verheugt FW, Col J, Materne P, Monassier JP, Geslin PG, Metzger J, Raynaud P, Foucault J, de Zwaan C Thrombolysis in patients with unstable angina improves the angiographic but not the clinical outcome. Results of UNASEM, a multicenter, randomized, placebo-controlled, clinical trial with anistreplase. *Circulation* 1992;86:131-7 [[1617766](#)]

TAUSA, 1994:

Ambrose JA, Almeida OD, Sharma SK, Torre SR, Marmur JD, Israel DH, Ratner DE, Weiss MB, Hjendahl-Monsen CE, Myler RK Adjunctive thrombolytic therapy during angioplasty for ischemic rest angina. Results of the TAUSA Trial. TAUSA Investigators. Thrombolysis and Angioplasty in Unstable Angina trial. *Circulation* 1994;90:69-77 [[8026054](#)]

Topol, 1988:

Topol EJ, Nicklas JM, Kander NH, Walton JA, Ellis SG, Gorman L, Pitt B Coronary revascularization after intravenous tissue plasminogen activator for unstable angina pectoris: results of a randomized, double-blind, placebo-controlled trial. *Am J Cardiol* 1988;62:368-71 [[2970776](#)]

TIMI 3A, 1993:

Early effects of tissue-type plasminogen activator added to conventional therapy on the culprit coronary lesion in patients presenting with ischemic cardiac pain at rest. Results of the Thrombolysis in Myocardial Ischemia (TIMI IIIA) Trial. *Circulation* 1993 Jan;87:38-52 [[8419023](#)]

Nicklas, 1989:

Nicklas JM, Topol EJ, Kander N, O'Neill WW, Walton JA, Ellis SG, Gorman L, Pitt B Randomized, double-blind, placebo-controlled trial of tissue plasminogen activator in unstable angina. *J Am Coll Cardiol* 1989;13:434-41 [[2492325](#)]

Gold, 1987:

Gold HK, Johns JA, Leinbach RC, Yasuda T, Grossbard E, Zusman R, Collen D A randomized, blinded, placebo-controlled trial of recombinant human tissue-type plasminogen activator in patients with unstable angina pectoris. *Circulation* 1987 Jun;75:1192-9 [[3105913](#)]

Williams, 1990:

Williams DO, Topol EJ, Califf RM, Roberts R, Mancini GB, Joelson JM, Ellis SG, Kleiman NS Intravenous recombinant tissue-type plasminogen activator in patients with unstable angina pectoris. Results of a placebo-controlled, randomized trial. *Circulation* 1990 Aug;82:376-83 [[2115407](#)]

Freeman, 1992:

Freeman MR, Langer A, Wilson RF, Morgan CD, Armstrong PW Thrombolysis in unstable angina. Randomized double-blind trial of t-PA and placebo. *Circulation* 1992;85:150-7 [[1728444](#)]

van der Brand, 1991:

van den Brand M, van Zijl A, Geuskens R, de Feyter PJ, Serruys PW, Simoons ML Tissue plasminogen activator in refractory unstable angina. A randomized double-blind placebo-controlled trial in patients with refractory unstable angina and subsequent angioplasty. *Eur Heart J* 1991;12:1208-14 [[1782951](#)]

charbonnier, 1992:

Charbonnier B, Bernadet P, Schiele F, Thery C, Baudouy M, Bauters C [Intravenous thrombolysis by recombinant plasminogen activator (rt-PA) in unstable angina. A randomized multicenter study versus placebo] *Arch Mal Coeur Vaiss* 1992;85:1471-7 [[1297297](#)]

Ardissino, 1990:

Ardissino D, Barberis P, De Servi S, Mussini A, Rolla A, Visani L, Specchia G Recombinant tissue-type plasminogen activator followed by heparin compared with heparin alone for refractory unstable angina pectoris. *Am J Cardiol* 1990;66:910-4 [[2121016](#)]

TIMI 3B, 1995:

Anderson HV, Cannon CP, Stone PH, Williams DO, McCabe CH, Knatterud GL, Thompson B, Willerson JT, Braunwald E One-year results of the Thrombolysis in Myocardial Infarction (TIMI) IIIB clinical trial. A randomized comparison of tissue-type plasminogen activator versus placebo and early invasive versus early conservative strategies in unstable angina and non-Q wave myocardial infarction. *J Am Coll Cardiol* 1995;26:1643-50 [[7594098](#)]

4 surgery

| Trial | Treatments | Patients | Trials design and methods |
|--|--|-----------------------------------|-------------------------------|
| surgery vs medical treatment | | | |
| VA cooperative , 1987 n=231/237 follow-up: 2 years (5,10 years) | coronary-artery bypass surgery plus medical therapy versus medical therapy alone | men with unstable angina pectoris | Parallel groups open US |

References

VA cooperative, 1987:

Luchi RJ, Scott SM, Deupree RH Comparison of medical and surgical treatment for unstable angina pectoris. Results of a Veterans Administration Cooperative Study. *N Engl J Med* 1987 Apr 16;316:977-84 [[2882420](#)]

Parisi AF, Khuri S, Deupree RH, Sharma GV, Scott SM, Luchi RJ Medical compared with surgical management of unstable angina. 5-year mortality and morbidity in the Veterans Administration Study. *Circulation* 1989 Nov;80:1176-89 [[2680157](#)]

Scott SM, Deupree RH, Sharma GV, Luchi RJ VA Study of Unstable Angina. 10-year results show duration of surgical advantage for patients with impaired ejection fraction. *Circulation* 1994 Nov;90:III20-3 [[7955237](#)]

Sharma GV, Deupree RH, Khuri SF, Parisi AF, Luchi RJ, Scott SM Coronary bypass surgery improves survival in high-risk unstable angina. Results of a Veterans Administration Cooperative study with an 8-year follow-up. Veterans Administration Unstable Angina Cooperative Study Group. *Circulation* 1991 Nov;84:III260-7 [[1934418](#)]

5 About TrialResults-center.org

TrialResults-center is an innovative knowledge database that collects the results of RCTs and provides dynamic interactive systematic reviews and meta-analysis in the field of all major heart and vessels diseases.

The TrialResults-center database provides a unique view of the treatment efficacy based on all data provided directly from clinical trial results, offering a valuable alternative to personal bibliographic search, published meta-analysis, etc. Furthermore, it would allow comparing easily the various concurrent therapeutic for the same clinical condition.

Rigorous meta-analysis method is used to populate TrialResults-center: widespread search of published and non published trials, study selection using pre-specified criteria, data extraction using standard form.

TrialResults-center is continually updated on a weekly basis. We continually search all new results (whatever their publication channel) and these news results are immediately added to the database with a maximum of 1 week.

TrialResults-center is non-profit and self-funded.