Data Supplements: 2015 Focused Update on Primary PCI for Patients With STEMI

Data Supplement 1-A. Observational Studies Comparing Culprit Artery-Only Revascularization Versus Multivessel PCI (Section 2)

Study Acronym Author Year	Aim of Study; Study Type; Study Size (N)	Patient Population	Primary Endpoint and Results	Relevant 2° Endpoint (if any); Study Limitations; Adverse Events and Summary
Iqbal MB, et al., 2014 (1) 25371542	Aim: To investigate mortality for COR vs. MV PCI at the time of PPCI for patients presenting with STEMI Study type: Observational. Used multivariate analysis and propensity matching Size: 3984 (MV PCI at time of PPCI=555; COR=3429)	Inclusion criteria: • STEMI and PPCI • MVD defined as >50% stenosis in ≥2 epicardial coronary arteries Exclusion criteria: • LM >50% stenosis • Cardiogenic shock	1° endpoint: 1-y mortality • Total study population: 7.4% (COR) vs.10.1% (MV) (p=0.031) • Adjusted HR Total population: 0.65 (95% CI: 0.47-0.91; p=0.011) • Propensity matched cohort: 164/2418 (6.8%) vs. 41/403 (10.2%) , p=0.059 • Adjusted propensity matched cohort HR: 0.64 (95% CI: 0.45-0.90; p=0.010)	• Inverse probability treatment weighted analyses also confirmed COR as an independent predictor for reduced in-hospital MACE (odds ratio, 0.38; 95% CI, 0.15–0.96; p=0.040) and survival at 1 year (hazard ratio, 0.44; 95% CI, 0.21–0.93; p=0.033).
Santos AR, et al., 2014 (2) 24502933	Aim: To assess the impact of a MV PCI at the time of PPCI on in-hospital morbidity and mortality in patients with STEMI undergoing PPCI Study type: Observational: Portuguese Society of Cardiology's Registry of Acute Coronary Syndromes (ACS) Size: 257 (MV PCI at time of PPCI 77 vs. COR 180)	Inclusion criteria: • STEMI • Enrolled in Portuguese Society of Cardiology Registry • MVD defined as ≥50% Exclusion criteria: • Staged MV PCI • History of prior CABG	1° endpoint : In-hospital mortality COR vs. MV PCI at time of PPCI: • In-hospital Mortality: 14/180 (7.8%) vs. 2/77 (2.6%), p=NS • Adjusted mortality OR: 12.92, 95% CI 0.67-248.4, p=0.09	
Jeger R, et al., 2014 (3) 24461983	Aim: To assess whether MV PCI at time of PPCI vs. COR in patients with STEMI and MVD influences 1-y outcome Study type: Observational: Swiss Nationwide Acute Myocardial Infarction in Switzerland Plus Registry (AMIS)	Inclusion criteria: • STEMI or new LBBB • MVD defined as a ≥50% in ≥2 different major epicardial coronary arteries and/or involving the LM. • Written informed consent to enroll	1° endpoint: 1-y all-cause mortality MV PCI 12/442 (2.7%) vs COR: 40/1467 (2.7%), p>0.99	• MACCE at 1 y (all-cause death, re-MI, any cardiac re- intervention, re-hospitalization due to any cardiovascular diagnosis, and CVA): Adjusted OR for MV PCI vs COR=0.69, 95% CI 0.51–0.93, p=0.017

	Size: 1909 (MV PCI at time of PPCI 442 vs. COR 1467)	in registry. Exclusion criteria: • Absence of follow-up data		
Manari A, et al., 2014 (4) 24403174	Aim: To examine the differences in cardiac outcomes for patients with STEMI and MVD as a function of whether they underwent COR or MV PCI, either at the time of PPCI or as a staged procedure. Study type: Observational retrospective: REAL registry Size: 2061 (MV PCI at time of PPCI 367, Staged MV PCI within 60 d 988, COR 706)	Inclusion criteria: • STEMI and MVD enrolled in REAL registry Exclusion criteria: • N/A	1° endpoint: Mortality at 30 d and 2 y COR vs. staged MV PCI • 30-d mortality: adjusted HR: 2.81 (95% CI: 1.34-5.89; p=0.006) • 2-y mortality: adjusted HR: 1.93 (95% CI: 1.35-2.74; p=0.0002) MV PCI at time of PPCI vs. staged MV PCI: • 30-d mortality adjusted HR: 2.58 (95 % CI: 1.06-6.26; p=0.03) • 2-y adjusted HR: 1.08 (95% CI: 0.64-1.82; p=0.76) COR vs. MV PCI at time of PPCI • 2-y unadjusted mortality:127/706 (18.0%) vs. 26/367 (7.1%), p=0.0002	• Study looked at timing of MV PCI and showed that staged MV PCI was associated with better outcomes than either COR or MV PCI at the time of PPCI
Jaguszewski M, et al., 2013 (5) 24384288	Aim: To compare the outcomes with MV PCI at the time of PPCI with COR Study type: Observational: Swiss Nationwide Acute Myocardial Infarction in Switzerland Plus Registry (AMIS) Size: 4941 (MV PCI at time of PPCI-1108 vs. COR-3833)	Inclusion criteria: • STEMI • MVD: stenosis ≥50% in at least two of three major coronary arteries and/or involving the LM (in pts with prior CABG) Exclusion criteria: • N/A	1° endpoint: In-hospital mortality MV PCI at time of PPCI vs. COR: • 81/1108 (7.3%) vs. 168/3833 (4.4%), p<0.001 • Low risk pts: 2.0% vs.2.0% (p=1.00) • High risk pts: 22.2% vs. 21.7% (p=1.00)	
Bauer T, et al., 2013 (6) 22192297	Aim: To evaluate the impact of MV-PCI during a single procedure on in-hospital outcomes of patients with MVD presenting with ACS Study type: Observational: Euro Heart Survey Registry with STEMI Size: 2537 (MV PCI during a single procedure 419 vs. COR 2118)	Inclusion criteria: • Hemodynamically stable patients with ACS • MVD defined as ≥2 vessels with ≥70% stenosis • Undergoing PCI Exclusion criteria: • N/A	1° endpoint: In-hospital mortality MV PCI during single procedure vs. COR: • 6/419 (1.4%) vs. 72/2118 (3.4%), p=0.03 • In-hospital mortality adjusted OR: 0.48 (95% CI: 0.21-1.13; p=0.73)	• Non-fatal MI: higher with MV PCI (8.8% vs.1.6%, p<0.0001)
Dziewierz A, et al., 2010 (7) 20643243	Aim: To assess the impact of MV PCI at time of PPCI vs COR in pts with STEMI and MVD Study type: Observational: Euro-Transfer Registry	Inclusion criteria: • Patients with STEMI included in Euro-transfer registry • MVD on cath Exclusion criteria: • N/A	1° endpoint: 1-y mortality MV PCI at time of PPCI vs. COR • 11/70 (15.7%) vs. 57/707 (8.1%), p=0.043 • Adjusted OR: 2.04 (95% CI: 0.89–4.66; p=0.09)	• 30-d mortality: 12.9% vs.5.9% (p=0.039) • Adjusted 30-d mortality: OR: 2.42 (95% CI: 0.96-6.06; p=0.06)

	Size: 777(MV PCI at time of PPCI 70 vs. COR 707)			
APEX-AMI Toma M, et al., 2010 (8) 20530505	Aim: To evaluate the 90-d outcomes for MV PCI performed at the time of PPCI Study type: Observational: APEX AMI Size: 2201(MV PCI at time of PPCI 217 vs. COR 1984)	Inclusion criteria: • ≥18 y • Ischemic symptoms <6 h • STEMI undergoing PPCI • MVD with ≥70% stenosis of another major epicardial vessel and/or requiring PCI Exclusion criteria: • PCI following lytics • Limited IWMI • LM PCI	1° endpoint: 90-d mortality and composite of death, CHF, and cardiogenic shock MV PCI at time of PPCI vs. COR: • 90-d mortality: 27/217 (12.4%) vs. 111/1984 (5.6%) , p<0.001; Adjusted HR: 2.44, 95% CI 1.55–3.83, P <0.001 • Unadjusted 90-d death/CHF/shock 18.9% vs.13.1% (p=0.011); Adjusted HR 1.39 (95% CI: 0.96-2.01; p=0.083)	• Limited inclusion of only STEMI pts that met the APEX-AMI trial criteria.
Hannan EL, et al., 2010 (9) 20129564	Aim: To examine the differences in in-hospital and longer-term mortality for patients with STEMI and MVD as a function of whether they underwent COR or MV PCI, either at the time of PPCI or as a staged procedure Study type: Observational; NY State Registry Size: 4,024 (MV PCI at time of PPCI=503; Staged MV PCI =259; COR=3,521)	Inclusion criteria: • STEMI within 24 h undergoing PPCI • MVD • NY State resident Exclusion criteria: • Missing data on EF • Thrombolytic therapy • Shock • Prior CABG	1° endpoint: In hospital, 12-, 24-, and 42-mo mortality For MV PCI at time of PPCI vs. COR: • In-hospital mortality: 3.4% vs.2.0% (p=0.14) • 12-mo mortality: 7.1% vs.5.5%, (p=0.23) • 24-mo mortality: 8.6% vs.6.6% (p=0.17) • 42-mo mortality: 11.7% vs. 10.7% (p=0.23) • Propensity matched 42-mo mortality: 59/503 vs. 54/503 Staged MV PCI during index admission vs. COR: • In-hospital mortality: 1.2% vs.1.9% (p=0.48) • 12-mo mortality: 3.9% vs.5.5% (p=0.53) • 24-mo mortality: 6.3% vs.7.4% (p=0.71) • 42-mo mortality: 6.3% vs.8.4% (p=0.72) For Staged MV PCI within 60 d vs. COR: • 12-mo mortality:1.3% vs.3.3% (p=0.04) • 24-mo mortality: 3.7% vs.4.3% (p=0.21) • 42-mo mortality: 5.6% vs.7.4% (p=0.17)	• Used propensity matched data to evaluate the outcome of MV PCI at various time points compared with COR. • Of note, for the subgroup of patients without shock, low EF or arrhythmias, MV PCI at the time of PPCI as compared with COR resulted in a higher in hospital mortality (2.4% vs.0.9%,p=0.04) and trends toward higher 24-mo (7.2% vs.4.9%, p=0.07) and 42-mo (10.4% vs.6.7%, p=0.08) mortality
Cavender MA et al.,	Aim: To examine the outcomes of patients	Inclusion criteria:	1° endpoint: In-hospital mortality.	• Bleeding (non-shock patients): 6.71%

2009 (10) 19660603	with STEMI undergoing MV PCI at time of PPCI vs. patients undergoing COR Study type: Observational: NCDR Registry Size: 28,936 (MV PCI at time of PPCI 3,134 vs. COR 25,802)	• STEMI treated with PPCI • ≥1 additional major artery with significant stenosis. Exclusion criteria: • PCI of LM • Staged PCI in hospital • Recent thrombolytics	MV PCI at time of PPCI vs. COR: • In hospital mortality: 246/3134 (7.85%) vs. 1321/25802 (5.12%), p<0.01 • Patients without shock: 3.26% vs.2.53% (p=0.09); Adjusted mortality: OR=1.23 (95% CI: 0.94-1.61; p=1.23) • Patients with shock: 36.49% vs.27.77% (p≤0.01); Adjusted mortality: OR=1.54 (95% CI: 1.22-1.95; p<0.01)	(MV at time of PPCI) vs.5.30% (COR), p<0.01 • Trend towards more renal failure with MV PCI at time of PPCI 2.31% vs.1.81% (p=0.09) • Very large registry also analyzed outcomes according to presence or absence of shock.
Varani E, et al., 2008 (11) 18798239	Aim: To examine a strategy of COR vs.MV-PCI on clinical outcomes in a cohort of patients with STEMI treated with PPCI and compare the outcomes of MVD patients according to the type of revascularization (MV PCI at the time of PPCI vs. staged MV PCI vs. COR) Study type: Observational: single center Size: Total=399. MV PCI before discharge 243 (divided into groups: MV PCI at time of PPCI= 147; MV PCI within 24 h =48; and MV PCI after 24 h but before before discharge=48); COR=156	Inclusion criteria: • Ongoing symptoms within 24 h • STEMI • MVD (≥2 major epicardial coronary arteries or their major branches with stenosis ≥70%) Exclusion criteria: • PCI for acute occlusion after angiography	Endpoints: Death from any cause and any revascularization. Time point not specified. In-hospital mortality for COR vs. MV PCI at time of PPCI: 8/156 (5.1%) vs. 12/147 (8.2%), p<0.05 COR vs. MV PCI at time of PPCI vs. MV PCI within 24 h vs. MV PCI before discharge • 6.6% vs. 9.9% vs. 2.1% vs. 2.1% (p=0.066 for overall comparison) • excluding pts with shock or CHF: 6.3% vs.3.3% vs.2.1% vs.2.1% (p=0.257)	Complete revascularization in 46% of patients with MVD
Qarawani D, et al., 2008 (12) 17428557	Aim: To compare outcomes with two strategies used for treating MVD and acute MI Study type: Observational: Single center Size: 120 (MV PCI at time of PPCI 95 vs. COR 25)	Inclusion criteria: • Prolonged >30 min ischemic chest pain • Symptom onset <12 h • STEMI • MVD defined as >70% stenosis of ≥1 additional coronary artery Exclusion criteria: • Cardiogenic shock • LM ≥50%	1° endpoint: In-hospital MACE (re-ischemia, re-MI, acute CHF and mortality) MV PCI vs. COR: • 16.7% vs. 52%, p=0.0001. • Adjusted OR for In-hospital MACE:14.68, 95% CI: 3.03–71.12, p=0.001	• In-hospital mortality: 4.2% vs.4.0%, p=NS • 1-year mortality for MV PCI vs. COR: 9/95 (9.5%) vs. 2/25 (8.0%), p=0.06 • MV PCI associated with improved hospital survival when compared with COR even after adjusting for other factors • MV PCI had higher rates of transient renal failure (8.4% vs.4.0%, p=0.01) and trend toward higher 1-y mortality (9.4% vs.8.0%, p=0.06)
Corpus RA, et al., 2004 (13) 15389238	Aim: To compare outcomes between an aggressive MV PCI strategy either at time of PPCI or before hospital discharge and COR Study type: Observational: Single Center Size: 506 (MV PCI 152 [Divided into 2 groups: MV PCI at the time of PPCI=26; staged in hospital PCI=126] vs.	Inclusion criteria: • STEMI • Symptom onset ≤ 12 h • MVD defined as ≥70% stenosis of ≥2 epicardial coronary arteries or their major branches Exclusion criteria: • PCI of vein graft or LM	1° endpoint: Numerous endpoints at 1 year MV PCI (either at time of PPCI or staged) vs COR: Death 11% vs 12 %, p=0.82 Re-infarction: 13.0% vs 2.8%, p<0.001 Revascularization: 25% vs 15%, p=0.007 MACE: 40% vs 28%, p=0.006	• Multivessel PCI was an independent predictor of MACE at 1 year (odds ratio=1.67, 95% CI 1.10-2.54, p=01).

	COR 354)	• PCI for acute occlusion after coronary angioplasty or arteriography; • MVD and staged revascularization procedures of the non-IRA after discharge from the hospital.	1-yr mortality MV PCI at time of PPCI vs staged MV PCI vs COR: 5/26 (19.2%) vs. 12/126 (9.5%) vs. 42/354 (11.9%), p=0.36	
Roe MT, et al., 2001 (14) 11448417	Aim: To determine the feasibility and safety of MV PCI at the time of PPCI Study type: Case Controlled Size: 158 (MV PCI at the time of PPCI 79 [Divided into 2 Groups: MV PCI at time of PPCI=68; Rescue PCI=11] vs. COR 79 ([PPCI 61,Rescue PCI=18])	Inclusion Criteria: • Patients with AMI undergoing PCI • ≥1 coronary stenosis ≥50% in a non-culprit vessel) Exclusion criteria: • PCI of branch vessels of IRA • PCI of LM	1° endpoint: Death, re-MI, repeat PCI or CABG at 6 mo MV PCI at time of PPCI vs. COR: 35.3% vs 27.9% p=NS	• Study found higher mortality for MV PCI vs. COR in the primary PCI group at 30 d but no difference in events at 6 mo • Study involved a mix of POBA and stents • 6-mo mortality for MV PCI at time of PPCI vs. COR: 19/79 (24.1%) vs.13/79 (16.1%), p=NS

Data Supplement 1-B. RCTs Comparing Culprit Artery-Only Revascularization Versus Multivessel PCI (Section 2)

Study Acronym Author Year	Aim of Study; Study Type; Study Size (N)	Patient Population	Study Intervention	Primary Endpoint and Results	Relevant 2° Endpoint (if any); Study Limitations; Adverse Events and Summary
DANAMI 3-PRIMULTI Engstrom T, et al., 2015 (15) (Not yet in PubMed)	Aim: To determine whether staged angiographic or FFR guided revasc in STEMI patients with MVD reduces the primary endpoint of all cause death, reinfarction and repeat revascularisation compared with COR Study type: Randomized Size: 627 (314 staged MV PCI; 313 COR)	Inclusion criteria: • STEMI ≤12 h • Successful IRA PPCI • >50% stenosis >2mm in non-IRA suitable for PCI Exclusion criteria: • Hemodynamic instability or ischemia in non IRA territory • CTO of non-IRA	Intervention: Complete in-hospital revasc with staged MV PCI for lesions >90% and staged FFR-guided MV PCI for lesions of 50- 90% severity(n=314) Comparator: COR (n=313)	1° endpoint: MACE at 12 mo (Death, MI, ischemia-driven revasc of non-IRA lesions) MV PCI vs. COR • 40/314 (13%) patients treated with staged MV PCI vs 68 of 313 (22%) patients treated with COR, p=0.004; (HR 0.56, 95% CI 0.38-0.83, p=0.001)	• 12-mo mortality: 15/314 (5%) vs. 11/313 (4%) • This study used FFR guidance for lesions of 50%-90% severity. • Benefit was driven by a significant reduction in ischemia-driven revascularization; death and MI rates were similar
CvLPRIT Gershlick AH, et al., 2015 (16) 25766941	Aim: To compare differences in outcome for patients with STEMI and MVD randomized to MV PCI or COR Study type: Randomized Size: 296 (MV PCI=150; COR=146)	Inclusion criteria: • STEMI <12 h • Referred for PPCI • MVD on cath with ≥1vessel >2mm in diameter with >70% stenosis in 1 plane or >50% stenosis in 2 planes • Non IRA suitable for stent implantation	Intervention: MV PCI either at time of PPCI or as a staged in-hospital procedure (n=150) Comparator: COR (n=146)	1° endpoint: Composite of death, re-MI, CHF and ischemia- driven revasc at 12 mo MV PCI vs. COR 10.0% vs.21.2% (HR: 0.45; 95% CI: 0.24-0.84; p=0.009)	• 65% of pts underwent MV PCI at time of PPCI • Benefit was driven by sum of individual endpoints; no statistically significant difference in outcome in individual components of primary endpoint • Total 12-mo mortality: 4/150 (2.7%) vs. 10/146 (6.9%) (HR: 0.38; 95% CI: 0.12- 1.20; p=0.09

		Exclusion criteria: • Indication for or contraindication to complete revasc • Prior Q wave MI • Prior CABG • Shock, VSD or Moderate to severe mitral regurgitation • Chronic kidney disease • Stent thrombosis • CTO of the only non-IRA			
PRAMI Wald DS, et al., 2013 (17) 23991625	Aim: To compare the outcomes of MV PCI at the time of PPCI with COR and an ischemia guided approach to non-culprit artery disease. Study type: Randomized Size: 465 (234 MV PCI at time of PPCI; 231 COR)	Inclusion criteria: • Acute STEMI (incl LBBB) • Successful PPCI • MVD with ≥50% stenosis in ≥1 other artery suitable for PCI Exclusion criteria: • Shock, • Prior CABG, • LM or ostia of both LAD and circumflex with >50% stenosis • CTO of non-IRA	Intervention: MV PCI at the time of PPCI (n=234) Comparator: COR with ischemia guided approach to non-culprit artery disease (n=231)	1° endpoint: MACE: (death from cardiac causes, nonfatal MI, or refractory angina). Results assessed after mean f/u of 23 mo MV PCI at the time of PPCI vs. COR • 9.0% vs.22.9%, (HR 0.35, 95% CI 0.21–0.58, <0.001)	• Trial stopped early by DSMB • HR for components of primary endpoint (MV PCI vs PPCI only): o Death from cardiac causes: 0.34 (95% CI, 0.11 to 1.08) o Non-fatal MI: 0.32 (95% CI, 0.13 to 0.75) o Refractory angina: 0.35 (95% CI, 0.18 to 0.69) o All-cause mortality: 12/234 (5.1%) vs 16/231 (6.9%), p=NS
Dambrink JH, et al., 2010 (18) 20542783	Aim: To compare effect of early invasive FFR guided management vs. COR and ischemia-guided management on LV EF Study type: Randomized Size: 121 (FFR-guided MV PCI 80; COR 41)	Inclusion criteria: • STEMI patients undergoing successful PPCI • MVD • with ≥1 additional major artery or branch • with ≥50 % disease and at least 2.5 mm diameter Exclusion criteria: • Urgent indication for additional revasc • >80 y • CTO of non IRA • Prior CABG • LM ≥50 %, • Restenotic • lesions in non-IRA • Chronic atrial fibrillation, • Limited life expectancy • Other factors that made complete follow-up unlikely.	Intervention: PPCI and elective (within 3 wk) FFR guided management of non IRA disease (n=80) Comparator: COR with conservative ischemia- guided management of non IRA (n=41)	1° endpoint: EF at 6 mo FFR guided staged PCI vs. COR and ischemia-guided approach: EF 59± 9% vs. 57± 9%, p=0.362	• MACE at 6 mo: 21% vs. 22%, p=0.929 • MACE at 3 years: 35.4% vs 35.0%, p=0.96 • Death or MI at 3 years: 20.3% vs 0%, p=0.002 • Death at 3 years: 2/80 vs. 0/41

Politi L, et al., 2010 (19) 19778920	Aim: To compare long-term outcomes of three different strategies during PPCI in patients with STEMI and MVD: COR vs. staged MV PCI vs. MV PCI at the time of PPCI Study type: Randomized Size: 214 (65 MV PCI at time of PPCI; 65 staged MV PCI; 84 COR)	Inclusion criteria: • Chest pain within 12 h • STEMI Exclusion criteria: • Cardiogenic shock • LM ≥50% • Prior CABG • Severe valvular heart disease • Unsuccessful PPCI	Intervention: PPCI plus staged MV PCI: 65; MV PCI at the time of PPCI (n=65) Comparator: COR (n=84)	1° endpoint: MACE at mean f/u 2.5 y: (death, re-MI, re-hospitalization for ACS and repeat coronary revasc) MV PCI at the time of PPCI vs. staged MV PCI vs. COR: • 23.1% vs.20% vs.50% p<0.001 • Adjusted HR for MACE for MV PCI at the time of PPCI vs COR: 0.495, 95% CI 0.262 to 0.933, p=0.030 • Adjusted HR for MACE for Staged MV PCI vs COR: 0.377, 95% CI 0.194 to 0.732 p=0.004	• There were no differences in outcomes for staged MV PCI vs. MV PCI at time of PPCI but small number of enrolled patients • Mortality for MV PCI vs COR: 10/130 (7.7%) vs.13/84 (15.5%),
HELP-AMI, et al., Di Mario C, et al., 2004 (20) 16146905	Aim: To evaluate the efficacy of a complete revascularization strategy at the time of PPCI on reducing repeat revascularizations in follow-up Study type: Randomized Size: 69 (MV PCI at time of PPCI 52; COR 17)	Inclusion criteria: • Ischemic CP and STEMI • MVD on angiogram technically amenable to PCI Exclusion criteria: • Lesion in bypass grafts • Prior PCI or stent in segment with disease • Thrombolysis within past wk; • Shock • LM disease • Intention to treat more than 1 lesion • Calcified or tortuous vessels with lesions; side branch >2 mm	Intervention: MV PCI at time of PPCI (n=52) Comparator: COR then PCI of other vessels at operators discretion (n=17)	1° endpoint: Any repeat revasc at 1 y MV PCI at time of PPCI vs. COR: 17.3% vs.35.3%, p=0.174	• Very small study; Unbalanced randomization • 12-mo mortality: 1/52 (1.9%) vs. 0/17 (0%), p=0.754

ACS indicates acute coronary syndrome; AMI, acute myocardial infarction; BRAVE-2, Beyond 12 hours Reperfusion Alternative Evaluation trial; C, coronary; CAD, coronary artery disease; Cath, catheterization; CHF, congestive heart failure; CI, confidence interval; Contra, contraindications; COR, culprit artery-only (or infarct related artery-only) PCI; CR, complete revascularizations; CTO, chronic total occlusion; CV, cardiovascular; CVA, stroke; EF, ejection fraction; FFR, Fractional Flow Reserve; f/u, follow up; Fx, fibrinolysis; gp, group; HR, hazard ratio; IR, incomplete revascularization; IRA, infarct related artery; LAD, left anterior descending artery; LBBB, left bundle branch block; LM, left main; LV, left ventricle; MACE, major adverse cardiac events; MI, myocardial infarction; MVD; multivessel disease; MV PCI, multivessel PCI; NY, New York; Occ, occlusion; OR, odds ratio; PA, pulmonary artery; PCI, percutaneous coronary intervention; PCWP, pulmonary-capillary wedge pressure; POBA, balloon angioplasty; PPCI, primary PCI; pts., patients; RCT, randomized control trial; re-MI, recurrent MI; RCT; randomized controlled trial; revasc, revascularization; RR, relative risk; SK, streptokinase; SPECT, single-photon emission computed tomography; STE, ST elevation; STEMI, ST elevation myocardial infarction; sx, symptoms; THC, thrombocytopenia; TIA, transient ischemic attack; TIMI, thrombolysis in myocardial infarction; tPA, tissue plasminogen activator; TVR, target vessel revascularization; tx, treatment; and VSD, ventricular septal defect.

Data Supplement 2. RCTs for Aspiration Thrombectomy (Section 3)

Study Acronym Author Year	Aim of Study; Study Type; Study Size (N)	Patient Population	Study Intervention	Primary Endpoint and Results	Relevant 2° Endpoint (if any); Study Limitations; Adverse Events and Summary
TOTAL Jolly SS, et al., 2015 (21) 25853743	Aim: To assess whether thrombus aspiration reduces MACE in patients with STEMI Study type: Randomized Size: 10,732 (thrombectomy 5372, PCI alone 5360);	Inclusion criteria: • Symptoms of myocardial ischemia lasting for ≥ 30 min • Definite ECG changes indicating STEMI • Patients referred for primary PCI • Randomized within 12 h of symptom onset and prior to diagnostic angiography Exclusion criteria: • Prior CABG • Life expectancy <6 mo due to non-cardiac condition • Treatment with fibrinolytic therapy for qualifying index STEMI event	Intervention: Thrombus aspiration before PCI (5033) Comparator: PCI alone (5030)	1° endpoint: Composite of CV death, re-MI, cardiogenic shock, NYHA heart failure within 180 d Thrombectomy vs PCI alone: 6.9% vs. 7.0% (HR: 0.99; 95% CI: 0.85-1.15; p=0.86)	• Safety endpoint: Stroke within 30 d: thrombectomy 0.7% vs. 0.3% PCI alone (HR: 2.06; 95% CI: 1.13-3.75; p=0.02) • CV death: thombectomy 3.1% vs. 3.5% PCI alone (HR: 0.90; 95% CI 0.73-1.12; p=0.34). • Primary outcome + stent thrombosis +TVR: thrombectomy 9.9% vs. 9.8% PCI alone, (HR: 1.00; 95% CI: 0.89-1.14; p=0.95). Summary: • No group differences with respect to re-MI, shock, NYHA heart failure, stent thrombosis, TVR, major bleeding, net clinical benefit (primary efficacy outcome or stroke). • No differences in rate of primary outcome in pre-specified subgroups, including extent of thrombus burden. • Improved ST resolution and lower rates of distal embolization with thrombectomy • Bailout thrombectomy rate 7.1% among patients randomized to PCI alone. • No or possible thrombus present (TIMI thrombus grade 0-1) in 6.7% thrombectomy patients, 8.1% PCI-alone patients.

TASTE
Lagerqvist B, et al., 2014 (22)
25176395
	Aim: To assess if thrombus aspiration reduces mortality in STEMI pts at 1 y in the TASTE study
	
	Study type: Randomized
	
	Size: 7244 (3621 thrombectomy, 3623 PCI alone)
		Inclusion criteria:
		• Chest pain, at least for 30 min, onset of sx to admission <24 h
		• STEMI or LBBB
		
		Exclusion criteria:
		• Need for CABG
		• Previous randomization in TASTE trial
			Intervention: Thrombus aspiration before PCI (3621)
			
			Comparator: PCI only (3623)
				1° endpoint: N/A (previously reported in TASTE)	• Events at 1 year f/u:
					  • Death from any cause 5.3% vs. 5.6% (HR: 0.94; 95% CI: 0.78-1.15; p=0.57),
					  • Rehospitalization for MI 2.7% vs. 2.7% (HR: 0.97; 95% CI: 0.73-1.28; p=0.81), stent thrombosis 0.7% vs. 0.9% (HR: 0.84; 95% CI: 0.50-1.40; p=0.51)
					  • Incidence of composite of death, rehospitalization for MI, or stent thrombosis: 8.0% v. 8.5% (HR: 0.94; 95% CI: 0.8-1.11; p=0.48).
					• Outcome events were recorded on the

					basis of registry data and were not systematically adjudicated (ascertainment of outcome events may have been less accurate than a RCT). Results cannot necessarily be extrapolated to very high-risk pts who would not have been eligible for inclusion.
TASTE Frobert O et al., 2013 (23) 23991656	Aim: To assess if thrombus aspiration reduces mortality in STEMI pts. Study type: Randomized Size: 7244 (3621 thrombectomy, 3623 PCI alone)	Inclusion criteria: • Chest pain, at least for 30 min • Onset of sx to admission<24 h • STEMI or LBBB Exclusion criteria: • Need for CABG • Previous randomization in TASTE trial	Intervention: Thrombus aspiration before PCI (3621) Comparator: PCI only (3623)	1° endpoint: All-cause mortality at 30 d Thrombus aspiration vs PCI only: • 2.8% vs 3.0%; HR: 0.94; 95% CI: 0.72-1.22; p=0.63	• Rate of rehospitalization for recurrent MI at 30 d : HR:0.61; 95% CI:0.34-1.07; p=0.09 • Rate of stent thrombosis: HR: 0.47; 95% CI: 0.20-1.02; p=0.06). • TVR did not differ between groups • Bias due to the treating physician being aware of the group to which pt was assigned and entering the angiographic variables. No adjudication of events and no blinded review of angiograms
INFUSE-AMI Stone GW, et al., 2012 (24) 22447888	Aim: To evaluate reduction of infarct size by IC abciximab, manual aspiration thrombectomy or both (with bivalirudin anticoagulation) Study type: Randomized, 2x2 factorial design Size: 353 with evaluable MRI in thrombectomy arms (thrombectomy=174; no thrombectomy=179)	Inclusion criteria: • STEMI >30 min and ≥1 mm • PPCI sx-onset-to-device time of ≤5 h Exclusion criteria: • Prior MI, CABG, or LAD stent • Shock or CPR • Prior lytic or IIb/IIIa inhibitor for the present admission	Intervention: Thrombectomy (174) Comparator: No thrombectomy (179)	1° endpoint: Infarct size at 30 d as assessed by cardiac MRI Thrombectomy vs no thrombectomy: Infarct size 17.0% vs 17.3% (p=0.51)	• There were also no significant differences in absolute infarct mass or abnormal wall motion score
EXPIRA Sardella G, et al., 2009 (25) 19161878	Aim: To determine the effects of manual thrombectomy device on myocardial perfusion and infarct size assessed by CE-MRI Study type: Randomized Size: 175	Inclusion criteria: • 1st STEMI <9 h from sx onset • Infarct-related artery ≥2.5 mm in diameter • Thrombus score ≥3 • TIMI flow grade ≤1 Exclusion criteria: Cardiogenic shock, 3 vessel/ left main disease, TIMI >0-1, TS <3, contra to GPIIb/IIIa	Intervention: Manual thrombectomy-PCI (88) Comparator: PCI alone (87)	1° endpoint: Occurrence of final myocardial blush grade ≥2 Manual thrombectomy vs.PCI alone 88% vs. 60%; p=0.001	• Rate of ST resolution >70%; (manual thrombectomy-PCI vs. PCI [64% vs.39%; p=0.001]) • Cardiac death at 9 mos lower with manual thrombectomy-PCI (p=0.02) • CE-MRI substudy: presence and extent of MVO in acute phase (significantly lower with manual thrombectomy-PCI) and infarct size extent at 3 mo (significant reduction with manual thrombectomy-PCI) • Single center experience with small no. of pts.

TAPAS Vlaar PJ, et al., 2008 (26) 18539223	Aim: To determine cardiac death or reinfarction rate at 1y Study type: Randomized Size: 1071	Inclusion criteria: • AMI sx >30 min • Time from sx onset <12 h, STE >0.1mV in ≥2 leads Exclusion criteria: • Rescue PCI after thrombolysis • Known concomitant disease with life expectancy <6 mo	Intervention: Thrombus aspiration (535); 1 y f/u (530) Comparator: PCI (536); 1 y f/u PCI (530)	1° endpoint: Combined cardiac death or non-fatal re-MI at 1y; Thrombus aspiration vs. PCI alone: 5.6% vs.9.9% [HR: 1.81; 95% CI: 1.16-2.84; p=0.009]	• 1 y cardiac death: Thrombus aspiration vs. PCI:3.6% vs.6.7% [HR: 1.93; 95% CI: 1.11-3.37; p=0.02] • Limited power to assess clinical outcome. No systematic measurement of infarct size or LVF performed.
Svilaas T, et al., 2008 (27) 18256391	Aim: To assess whether manual thrombus aspiration is superior to conventional treatment during primary PCI Study type: Randomized Size: 1071	Inclusion criteria: • AMI sx >30 min • Time from sx onset <12 • STE >0.1 mV in ≥2 leads Exclusion criteria: • Rescue PCI after thrombolysis • Known concomitant disease with life expectancy <6 mo	Intervention: Thrombus aspiration (535) Comparator: PCI alone (536)	1° endpoint: Post procedure myocardial blush grade of 0 (no myocardial blush) or 1 (minimal myocardial blush or contrast density). Thrombus aspiration vs. PCI alone: 17.1 % vs.26.3% [RR: 0.65; 95% CI: 0.51-0.83; p<0.001]	• Thrombus aspiration vs. PCI alone at 30-day: o Major bleeding: 3.8% vs.3.4%, RR: 1.11; 95% CI: 0.60-2.08; p=0.11 o Target vessel revascularization: 4.5% vs.5.8%, RR: 0.77; 95% CI 0.46-1.30; p=0.34), o Reinfarction: 0.8% vs.1.9%, RR: 0.40; 95% CI: 0.13-1.27; p=0.11, o Death:2.1% vs.4.0%, RR: 0.52; 95% CI 0.26-1.07; p=0.07 o MACE: 6.8% vs.9.4%, RR: 0.72; 95% CI: 0.48-1.08; p=0.12 • Single-center study using surrogate endpoints (myocardial blush grade and ECG variables); performed randomization prior to coronary angiography (selection bias since some patients did not undergo PCI/received alternative therapy)

CABG indicates coronary artery bypass graft; CE-MRI, contrast enhanced MRI; CI, confidence interval; cMRI, cardiac magnetic resonance imaging; Contra, contraindications; CrCl, creatinine clearance; CV, cardiovascular; ECG, electrocardiogram; EM, Export Medtronic; GP2B/3A, glycoprotein IIb/IIIa; Hgb, hemoglobin; Hosp., hospitalization; HR, hazard ratio; IC, intracoronary; ITT, intention-to-treat; LVF, Left ventricular function; MACE, major adverse cardiac events; MACCE, major adverse cardiac and cerebrovascular events; MI, myocardial infarction; MVO, microvascularobstruction; NYHA, New York Heart Association; OR, odds ratio; PCI, percutaneous coronary intervention; PL, platelet count; RCT, randomized controlled trial; RR, relative risk; STEMI, ST-elevation myocardial infarction; STR, ST-segment resolution; SVG, Saphenous venous graft; TIMI, Thrombolysis In Myocardial Infarction; TS, thrombus score; and TVR, target vessel revascularization.

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