

2014 SIHD Focused Update Data Supplements

(Section numbers correspond to the full-text guideline.)

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Data Supplement 1. Studies of Flow Reserve Assessment for Intermediate Coronary Lesions

Study Name	Study Type	Study Size	Inclusion/Exclusion Criteria	Primary Endpoint	Results/CABG P Values	Summary/Conclusions
DEFER (1) 11413082	RCT	325 pts	Elective PCI 3 groups based on </≥0.75 FFR (deferral, performance, and reference groups)	Absence of death, MI, PCI, CABG by 24 mo	Same event in pts with FFR ≥0.75 with PCI or deferred	In pts with SVCAD and no documented ischemia, FFR identifies those who benefit from PTCA.
DEFER (2) 17531660	RCT	325 pts	Elective PCI SVD with 3 groups (deferral, performance, and reference groups) based on </≥0.75 FFR	Absence of death, MI, PCI, CABG by 60 mo	Similar to 2-y follow-up No benefit with PCI if FFR ≥0.75	In pts with SVCAD and no documented ischemia, FFR identifies those who benefit from PTCA.
FAME (3) 19144937	RCT	1,005 pts (DES)	MVD PCI with angiography PCI only vs. angiography and FFR ≤0.80	1-y death, MI, or repeat revasc	18.3% in angiography group; 13.2% in FFR group (p=0.02)	FFR-guided PCI in pts with MVD improves 1-y composite endpoints: death, MI, or revasc.
FAME (4) 20537493	RCT	1,005 pts (DES)	Pts with MVD with angiography PCI only or angiography and FFR ≤0.80	1-y death, MI, or repeat revasc	22.4% in angiography group; 17.9% in FFR group (p=0.08)	FFR-guided PCI in pts with MVD improves 2-y composite endpoints: death, MI, or and revasc.
(FFR vs. IVUS) (5) 20723852	NR	167 pts	40% to 70% PCI of stenosis with IVUS MLA ≤4.0 cm ² or FFR ≤0.8	1-y death, MI, or repeat revasc	No difference: 3.6% FFR vs. 3.2% IVUS	No difference in events; more PCIs in IVUS group (91.5%) vs. FFR (33.7%) (p<0.001).
(LM) (6) 19327420	NR	142 consecutive pts	LM 30% to 60% or indeterminate. FFR <0.75 revasc recommended, >0.80 medical therapy recommended, or 0.75-0.80 either recommended	14-mo follow-up death, MI, CABG, PCI	13% medical vs. 7% revasc; Death or MI 6% vs. 7%, respectively	FFR may be helpful, but DM and dose of adenosine may influence decision.
(LM) (7) 19786633	NR	213 pts (209 with follow-up)	Equivalent LM FFR <0.80 surgery; 0.80 medical therapy	Event-free survival 3-y follow-up; 5 y estimated	74.2% medical therapy vs. 82.8% surgery (p=0.48)	FFR is beneficial for equivocal LM lesions in deciding need for revasc.
FAME 2 (8) 22924638	RCT	888 randomized pts	FFR ≤0.80 randomized to PCI vs. GDMT	Death, MI, or urgent revasc	12.7% medical therapy vs. 4.3% PCI (p<0.001)	Upfront stenting may prevent future urgent stenting; no decrease in death or MI with FFR-guided PCI.

CABG indicates coronary artery bypass graft; DEFER, Deferral Versus Performance of Balloon Angioplasty in Patients Without Documented Ischemia; DES, drug-eluting stent; DM, diabetes mellitus; FAME, Fractional Flow Reserve Versus Angiography for Multivessel Evaluation; FFR, fractional flow reserve; GDMT, guideline-directed medical therapy; IVUS, intravascular ultrasound; LM, left main; MI, myocardial infarction; MLA, minimal luminal area; mo, month(s); MVD, multivessel

disease; NR, nonrandomized; PCI, percutaneous coronary intervention; PTCA, percutaneous transluminal coronary angioplasty; pt(s), patient(s); RCT, randomized controlled trial; revasc, revascularization; SVCAD, single-vessel coronary artery disease; SVD, saphenous vein disease; and y, year(s).

Data Supplement 2. Chelation Therapy

Study Name, Author, Year	Aim of Study	Study Type	Study Size (N)	Study Intervention Group (n)	Study Comparat -or Group (n)	Patient Population		Study Intervention	Study Comparat or	Endpoints			P Values, OR: HR: RR and 95% CI	Study Limitations and Adverse Events
						Inclusion Criteria	Exclusion Criteria			Primary Endpoint (Efficacy) and Results	Safety Endpoint and Results	Secondary Endpoint and Results		
Guldager 1992 (9) 1556523	To assess the effect of chelation therapy on severe IC	RCT	153	75	78	All pts included in study >40 y and suffered from stable IC for at least 12 mo	Vascular surgery within the last 12 mo; ischemic rest pain or gangrene; moderate or severe venous insufficiency; renal insufficiency; DM; thyroid and parathyroid disorders; hepatic dysfunction; significant cardiopulmonary failure (e.g., MI in prior year); coexistent carcinomas; tuberculosis within last year; pregnancy; other conditions that	20 IV infusions of 3 g disodium EDTA	PC	3-mo pain-free walking distances, measured on a treadmill (chelation 95±48 m; PC 102±42 m); 6-mo pain-free walking distances, measured on a treadmill (chelation 95±47 m; PC 119±93 m); 3-mo maximal walking distance (chelation 162±101 m; PC 204±248 m); 6-mo maximal walking distance (chelation 180±150 m; PC 194±127 m)	Before treatment, a physical examination was performed together with the following serum and urine analyses: hemoglobin, thrombocytes, hematocrit APTT, prothrombin (Factors II, VII, and X), fasting glucose, fibrinogen, creatinine, albumin, calcium, phosphate, alkaline phosphatase, LDH, and urinary stick-test for protein, blood, and	ABI, BP, subjective evaluation, and lab tests (no differences between groups in any)	3-mo pain-free walking distance (RR: 0.98; 95% CI: 0.85, 1.13); 6-mo pain-free walking distance (RR: 1.04; 95% CI: 0.91, 1.19); 3-mo max walking distance (RR: 0.94; 95% CI: 0.82, 1.08); 6-mo max walking distance (RR: 0.96; 95% CI: 0.79, 1.16)	Lab tests on entry to study were in the normal range, and only alkaline phosphatase activity changed significantly during the study period. Alkaline phosphatase in EDTA-treated group decreased from mean value + SD of 175±55 U l ⁻¹ to 148 +/-42 U l ⁻¹ (p<0.001). Because of symptoms of hypocalcemia, 8 pts received IV calcium gluconate (EDTA 5 pts; PC 3 pts). 1 pt (EDTA group) showed subnormal calcium levels. In 3 pts (EDTA, 1 pt; PC 2 pts), creatinine levels increased after the 10th infusion, but normalized 8 d after cessation of treatment. In 11 pts (EDTA, 4 pts; PC, 7 pts), creatinine levels increased after the 20th infusion. Side effects were observed but were generally nonspecific and showed no

														preponderance in any groups. Incidence of phlebitis and pain at the infusion site, as well as GI side effects, were similar in the 2 groups. One pt developed Raynaud's phenomenon of 2 fingers after the 3rd EDTA treatment; symptoms persisted for 4 d then gradually disappeared spontaneously. EDTA pt developed localized dermatitis on nasal cheek fold after 6th infusion; this disappeared spontaneously after the treatment period.
van Rij 1994 (10) 8087928	To assess the effect of chelation therapy in pts with IC	RCT	32	15	17	Pts with angiographically confirmed PAD who did not have indications for invasive procedures; variation of <20% in measured walking distance over 3 separate assessments	Other debilitating disease affecting walking; younger than 45 y; DM; renal disease	20 IV infusions of 3 g disodium EDTA + IV vitamin supplements	PC + IV vitamin supplement s	Measured walking distance (end of treatment chelation 208 ± 135 m vs. PC 223 ± 149 m; 3-mo chelation 233 ± 135 m vs. PC 230 ± 130 m); subjective walking distance (end of treatment chelation 413 ± 775 m vs. PC 327 ± 461 m; 3-mo chelation 448 ± 556 m vs. PC 381 m ±473 m); ABI at rest (end of treatment chelation 0.7 ± 0.36 vs. PC 0.6 ± 0.15 ; 3-mo chelation 0.62 ± 0.15 vs. PC 0.58 ± 0.13) and	Lab monitoring of UA, hematology parameters, renal function, and serum Ca, Zn, Mg, and Fe; BP and heart rate monitoring during infusion therapy	Effect of chelation therapy on behavior and attitudes, as assessed by pt questionnaires (no significant difference noted between chelation and PC groups)	All p values for each primary outcome were >0.05 , except for 3 mo resting ABI measure	No complications were noted in either the chelation or placebo groups.

Knudtson 2002 (11) 11798370	To determine if current EDTA protocols have a favorable impact on exercise ischemia threshold and quality-of-life measures in pts with SIHD	RCT	84	41	43	Participants ≥21 y and have CAD proven by coronary angiography or documented MI and stable angina while receiving optimal MT. To qualify for randomization, pts were required to have a treadmill test, using a gradual ramping protocol, demonstrating at least 1 mm of horizontal or downsloping ST-segment depression from the isoelectric line 80 ms after	Exclusion criteria included planned revascularization, previous chelation therapy, evidence of HF, inability to walk on the treadmill, resting ECG changes that would interfere with ischemic assessment, abnormal renal or liver function, or untreated lipid abnormality at the time of randomization.	33 IV infusions of 3 g disodium EDTA + IV vitamin supplements	Placebo + IV vitamin supplement s	after ambulation (end of treatment chelation 0.32±0.18 vs. PC 0.34±0.17; 3-mo chelation 0.34±0.18 vs. PC 0.32±0.17)	The primary endpoint was the change in time to reach ≥1 mm of ST-segment depression at the 27-wk evaluation (chelation 572±172 s vs. PC 589±176 s).	Laboratory monitoring (renal function, Ca levels)	Peak VO ₂ (chelation change between baseline and 27 wk 84 mL/min (95% CI: 10, 159) vs. PC 40 mL/min (95% CI: 53, 134), time to reach anaerobic threshold (chelation change between baseline and 27 wk 31 s [95% CI: -11, 72] vs. PC 16 s [95% CI -27, 59])	All between-group comparisons were nonsignificant ($p>0.05$)	1 chelation pt was withdrawn from therapy because of elevation in serum creatinine. During first 10 treatments, pt serum creatinine level increased from 1.5 to 2.1 mg/dL (129 to 186 μmol/L respectively). Treatment was stopped, and serum creatinine level decreased to 1.6 mg/dL (138 μmol/L) after 10 wk. No other cause for the elevation in creatinine was found. In addition to the nonischemic events leading to discontinuation of therapy, 3 additional PC pts were hospitalized for nonischemic events: gout, lumbar back pain from a herniated disk, and GI bleeding. These events did not interfere with completion of the treatment phase. There were no electrolyte results out of normal range during the study.

TACT Lamas 2013 (12) 23532240	To determine if an EDTA-based chelation regimen reduces CV events	RCT	1,708	839	869	the J point. The study protocol required detection of ST-segment depression between 2-14 min from the onset of exercise.	Eligible pts were ≥ 50 y and experienced MI ≥ 6 wk before enrollment.	Pts ineligible if they were women of childbearing potential, had a serum creatinine level >2.0 mg/dL, platelet count $<100,000/L$, abnormal liver function studies, BP $>160/100$ mm Hg, past intolerance to the chelation or vitamin components, chelation therapy within 5 y, coronary or carotid revascularization planned or having taken place within 6 mo, cigarette smoking within	40 IV infusions of 3 g disodium EDTA + IV vitamin supplements + oral vitamin supplements	IV and PO placebos	Primary endpoint was a composite of death from any cause, reinfarction, stroke, coronary revascularization, or hospitalization for angina over a 5-y period, chelation (32.8% [95% CI: 29.1-36.5%]) vs. PC (38.5% [95% CI: 34.6-42.3%])	Safety monitoring included periodic physical examinations and laboratory assessments: glucose, calcium, renal function, hepatic function, and hematologic parameters. Pts had body weight assessed before infusions to determine whether there was fluid retention.	The composite of CV death, reinfarction, or stroke was a prespecified secondary endpoint (96 chelation pts [11%] and 113 PC pts [13%])	Primary outcome (HR: 0.82; 95% CI: 0.69-0.99; p=0.035). Secondary outcome (HR: 0.84; 95% CI: 0.64-1.11; p=0.22)	4 unexpected severe adverse events occurred that were possibly or definitely attributed to study therapy, 2 in the chelation group (1 death) and 2 in PC group (1 death). HF was reported in 57 chelation pts (7%) and 71 PC pts (8%) (p=0.28). 330 (0.60%) of 55,222 infusions administered at least 30 min too rapidly. Hypocalcemia, defined as calcium level <8.5 mg/dL before an infusion, was reported in 52 chelation pts (6.2%) and 30 PC pts (3.5%) (p=0.008). 1 pt had hypocalcemia associated with muscle cramping that led to ED visit.

							3 mo, active HF or HF hospitalization within 6 mo, or inability to tolerate 500-mL infusions/wk							
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ABI indicates ankle/brachial indices; APTT, activated partial thromboplastin time; BP, blood pressure; CAD, coronary artery disease; CI, confidence interval; CV, cardiovascular; DM, diabetes mellitus; ECG, electrocardiographic; ED, emergency department; EDTA, ethylenediaminetetraacetic acid; GI, gastrointestinal; HF, heart failure; HR, hazard ratio; IC, intermittent claudication; IV, intravenous; LDH, lactic dehydrogenase; m, meter(s); MI, myocardial infarction; mo, month(s); MT, medical therapy; OR, odds ratio; PAD, peripheral artery disease; PC, placebo; PO, per oral; pt(s), patient(s); RCT, randomized controlled trial; RR, relative risk; s, seconds; SIHD, stable ischemic heart disease; UA, unstable angina; wk, week(s); and y, year(s).

Data Supplement 3. External Enhanced Counterpulsation

Study Name, Author, Year	Aim of Study	Study Type	Study Size (N)	Study Intervention Group (n)	Study Comparator Group (n)	Patient Population		Study Intervention	Study Comparator	Endpoints			P Values, OR: HR: RR and 95% CI	Study Limitations and Adverse Events
						Inclusion Criteria	Exclusion Criteria			Primary Endpoint (Efficacy) and Results	Safety Endpoint and Results	Secondary Endpoint and Results		
Arora 1999 (13) 10362181	Evaluate ECCP in pts with angina	RCT	N=139	EECP (n=72)	Sham Control (n=67)	Age 21-81 y Canadian CV Class I, II, or III angina Documented CAD Positive ETT	MI or CABG in preceding 3 mo, cardiac catheterization in the preceding 2 wk, UA, CHF, or LVEF <30%, significant valvular disease, BP >180/100 mm Hg, permanent pacemaker or ICD, left main stenosis >50%, severe symptomatic PVD, history of varicosities, DVT, AF	Evaluate ECCP in pts with angina	RCT	N=139	EECP (n=72)	Sham Control (n=67)	Age 21-81 y Canadian CV Class I, II, or III angina Documented CAD Positive ETT	MI or CABG in preceding 3 mo, cardiac catheterization in the preceding 2 wk, UA, CHF, or LVEF <30%, significant valvular disease, BP >180/100 mm Hg, permanent pacemaker or ICD, left main stenosis >50%, severe symptomatic PVD, history of varicosities, DVT, AF were excluded
Braith 2010 (14) 20921442	To investigate the	RCT	N=42	EECP n=28	Sham Control n=14	Refractory chronic angina with	Absence of ST-segment depression during exercise testing; >75 y,	To investigate the	RCT	N=42	EECP n=28	Sham Control n=14	Refractory chronic angina with	Absence of ST-segment depression during exercise testing; >75 y,

	extracardiac effects of EECP on peripheral artery flow-mediated dilation				multivessel CAD	recent catheterization, CABG or PCI; arrhythmia; CHF; LVEF <30%; valvular disease, ICD discharge within past 6 mo, history of DVT, uncontrolled HTN, pregnancy, pulmonary congestion, hypotension	extracardiac effects of EECP on peripheral artery flow-mediated dilation					multivessel CAD	recent catheterization, CABG, or PCI, arrhythmia; CHF; LVEF <30%; valvular disease, ICD discharge within past 6 mo, history of DVT, uncontrolled HTN, pregnancy, pulmonary congestion, hypotension were excluded
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AF indicates atrial fibrillation; BP, blood pressure; CABG, coronary artery bypass graft; CAD, coronary artery disease; CHF, congestive heart failure; CI, confidence interval; CV, cardiovascular; DVT, deep vein thrombosis; EECP, external enhanced counterpulsation; ETT, exercise treadmill testing; HR, hazard ratio; HTN, hypertension; ICD, implantable cardioverter-defibrillator; LVEF, left ventricular ejection fraction; MI, myocardial infarction; mo, month(s); OR, odds ratio; PCI, percutaneous coronary intervention; pts, patients; PVD, peripheral vascular disease; RCT, randomized controlled trial; RR, relative risk; UA, unstable angina; wk, week(s); and y, year(s).

Data Supplement 4. Evidence for Survival Benefit After PCI or CABG (With LIMA Grafting to the LAD) in Patients With SIHD Who Are Receiving Medical Therapy and Are Suitable Candidates for Revascularization

Anatomic Subgroups	Evidence Supporting CABG for Survival	Evidence Supporting PCI for Survival	Evidence Supporting Superiority of Either CABG or PCI for Survival	Evidence Supporting Equivalence of CABG and PCI for Survival
Unprotected left main CAD	CASS Registry* (15,16) 7729018 2785870 CASS† (17) 7025604 VA Cooperative† (18,19) 791537 6979435 Yusuf et al.† (20) 7914958 Dzavik et al.* (21) 11431667	Bittl et al. (22) 23674397	<i>CABG better:</i> Wu* (23) 18805151 <i>PCI better: None found</i>	SYNTAX† (25) 20530001 LE MANST (26) 18237682 Boudriot et al.† (27) 21272743 Chieffo et al.* (28,29) 16717151 20630452 Lee et al.* (30) 16487857 Lee et al.§ (31) 20723848 Naik et al.§ (32) 19695542 White et al.* (33) 19463306 Palmerini et al.* (34) 16784920 Park et al.* (35) 20451344 Sanmartín et al.* (36) 17826380 Brener et al.* (37) 18178401 Mäkikallio et al.* (38) 18608116

3-vessel disease with or without proximal LAD disease	<p><i>For:</i></p> <p>Dzavik et al.* (21) 11431667 ECSS† (39) 3260659 Jones et al.* (40) 8622299 MASS II* (41) 20733102 Myers et al.† (42) 2648078 Smith et al.* (43) 16996946 SYNTAX†(24) 21697170 Weintraub (44) 22452338 Yusuf et al.† (20) 7914958</p>	<p><i>For:</i></p> <p>Dzavik et al.* (21) 11431667 Smith et al.* (43) 16996946</p> <p><i>Against:</i></p> <p>Boden et al.† (45) 17387127</p>	<p><i>CABG better:</i></p> <p>Bair et al.* (46) 17846308 Booth et al.† (47) 18606919 Hannan et al.* (48) 9935010 Hannan et al.* (49) 18216353 Jones et al.* (40) 8622299 MASS II* (41) 20733102 Malenka et al.* (50) 16159849</p>	Bravata et al.† (51) 17938385 Daemen et al.† (52) 18725490 Dzavik et al.* (21) 11431667 ERACI I† (53) 12527674 Mercado et al.† (54) 12643887 RITA I† (55) 8094826 Van Domburg et al.* (56) 11922644
2-vessel disease with proximal LAD disease	<p><i>For:</i></p> <p>ECSS† (39) 3260659 Jones et al.* (40) 8622299 Smith et al.* (43) 16996946 Yusuf et al.† (20) 7914958</p>	<p><i>For:</i></p> <p>Dzavik et al.* (21) 11431667 Jones et al.* (40) 8622299 Smith et al.* (43) 16996946</p> <p><i>Against:</i></p> <p>Boden et al.† (45) 17387127</p>	<p><i>CABG better:</i></p> <p>Hannan et al.* (48) 9935010 Hannan et al.* (49) 18216353 Hannan et al.* (57) 15917382 Jones et al.* (40) 8622299</p>	Berger et al.† (58) 11691521 ERACI I† (53) 12527674 Malenka et al.* (50) 16159849
2-vessel disease without proximal LAD disease	<p><i>For:</i></p> <p>Smith et al.* (43) 16996946</p>	<p><i>For:</i></p> <p>Jones et al.* (40) 8622299 Smith et al.* (43) 16996946</p> <p><i>Against:</i></p> <p>Boden et al.† (45) 17387127 Cecil et al.† (59) 18690768 Pitt et al.† (60) 10395630</p>	<p><i>CABG better:</i></p> <p>Bair et al.* (46) 17846308 Booth et al.† (47) 18606919 Dzavik et al.* (21) 11431667 Hannan et al.* (57) 15917382 Hannan et al.* (49) 18216353 Jones et al.* (40) 8622299</p>	Bravata et al.† (51) 17938385 Daemen et al.† (52) 18725490 Dzavik et al.* (21) 11431667 Jones et al.* (40) 8622299 Mercado et al.† (54) 12643887 Van Domburg et al.* (56) 11922644
1-vessel proximal LAD disease	<p><i>For:</i></p> <p>Smith et al.* (43) 16996946</p> <p><i>Against:</i></p> <p>Greenbaum et al.* (61) 11113406</p>	<p><i>For:</i></p> <p>Jones et al.* (40) 8622299 Smith et al.* (43) 16996946</p> <p><i>Against:</i></p> <p>Greenbaum et al.* (61) 11113406</p>	<p><i>CABG better:</i></p> <p>Hannan et al.* (48) 9935010</p>	Aziz et al.† (62) 17337458 Ben-Gal et al.* (63) 17126111 Bravata et al.† (51) 17938385 Cisowski et al.§ (64) 15531937 Diegeler et al.† (65) 12192015 Drenth et al.† (66) 15566914 Fraund et al.* (67) 15797053 Goy et al.† (68,69) 7911175 18755343 Greenbaum et al.* (61) 11113406 Hong et al.† (70) 15619278 Jaffery et al.† (71) 17300948 Jones et al.* (40) 8622299 Kapoor et al.† (72) 19463349 MASS I† (73) 7594092

1-vessel disease without proximal LAD involvement	<i>Against:</i> Jones et al.* (40) 8622299 Smith et al.* (43) 16996946 Yusuf et al.† (20) 7914958	<i>Against:</i> Jones et al.* (40) 8622299	<i>PCI better:</i> Hannan et al.* (48) 9935010 Jones et al.* (40) 8622299	Jones et al.* (40) 8622299
Multivessel CAD, DM present	<i>For:</i> MASSII† (74) 17184637 Sorajja et al.* (75) 16159837 <i>No benefit:</i> BARI 2D† (76) 19502645	<i>For:</i> MASSII† (74) 17184637 <i>No effect:</i> BARI 2D† (76) 19502645 Sorajja et al.* (75) 16159837	<i>CABG better:</i> BARI I† (77,78) 9323059 17433949 Brener et al.* (79) 15117846 Hlatky et al.† (80) 19303634 Javaid et al.* (81) 17846304 Malenka et al.* (50) 16159849 Niles et al.* (82) 11263600 Pell et al.* for 3-V CAD (83) 15209776 Weintraub et al.† (84) 9426011	ARTS I* (85) 11479249 Bair et al.* (46) 17846308 Barsness et al.* (86) 9355893 Bravata et al.† (51) 17938385 CARDia† (87) 20117456 Dzavik et al.* (21) 11431667 MASS II† (74) 17184637 Pell et al.* for 3-V CAD (83) 15209776

*Observational study, including articles on long-term follow-up, clinical trials not specified as randomized, comparative registry studies, comparative studies, prospective cohort studies, prospective observational studies, prospective registries, and prospective studies.

†Randomized controlled trials, including meta-analyses.

‡Reviews (systematic or not).

§Unknown study design.

ARTS indicates Arterial Revascularization Therapies Study Part; AWESOME, Angina With Extremely Serious Operative Mortality Evaluation; BARI I, Bypass Angioplasty Revascularization Investigation I; BARI 2D, Bypass Angioplasty Revascularization Investigation 2 Diabetes; CAD, coronary artery disease; CARDia, Coronary Artery Revascularization in Diabetes; DM, diabetes mellitus; ECSS, European Coronary Surgery Study; ERACI II, Argentine Randomized Trial of Percutaneous Transluminal Coronary Angioplasty versus Coronary Artery Bypass Surgery in Multivessel Disease II; LAD, left anterior descending; Le Mans, Study of Unprotected Left Main Stenting Versus Bypass Surgery; LIMA, left internal mammary artery; MASS, Medicine, Angioplasty, or Surgery Study; RITA, Randomised Intervention Treatment of Angina; SIHD, stable ischemic heart disease; SYNTAX, Synergy Between Percutaneous Coronary Intervention with TAXUS and Cardiac Surgery; V, vessel; and VA, Veterans Administration.

Data Supplement 5. RCTs Comparing CABG and DES

						Death %	MI %	Repeat Revascularization %	Primary Endpoint %		RR and 95% CI	Follow-Up in Months
Trial	No.	Age (y)	Female	CAD	Enrollment Period	CABG/PCI	CABG/PCI	CABG/PCI	CABG/PCI	CABG/PCI		
Hong et al. (70) 15619278	189	61	36%	SV	2003	2.9/0	2.9/1.7	5.9/1.7	D, MI, Rep Revasc	11.7/4.3	N/A	6
Leipzig (88) 19539141	130	66	30%	SV	2003-2007	0/0	7.7/1.5*	0/6.2	D+MI+Rep Revasc	7.7/7.7	N/A	12
SYNTAX (89,90) 19228612	1800	65	22%	MV	2005-2007	6.7/8.6	3.6/7.1	10.7/19.7	D+MI+CVA+Rep Revasc	20.2/28.0	Primary endpoint 12-mo follow-up; RR: 1.44; 95% CI: 1.15–1.81	36

FREEDOM (91) 18215589	1900	63	29%	MV	2005-2010	10.9/16.3	6.0/13.9	4.8/12.6	D+MI+CVA	18.7/26.6	RR: 0.74; 95% CI: 0.61–0.89	60
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*Statistically significant.

CABG indicates coronary artery bypass graft; CAD, coronary artery disease; CI, confidence interval; CVA, cerebrovascular accident; D, death; FREEDOM, Future Revascularization Evaluation in Patients with Diabetes Mellitus: Optimal Management of Multivessel Disease; DES, drug-eluting stent; MI, myocardial infarction; mo, month(s); MV, multivessel; N/A, not applicable; No., number of patients; PCI, percutaneous coronary intervention; RCT, randomized controlled trial; RR, relative risk; Rep Revasc, repeat revascularization; SV, single vessel; and SYNTAX, Synergy Between Percutaneous Coronary Intervention with TAXUS and Cardiac Surgery.

Data Supplement 6. Trials of PCI With CABG in Patients With Multivessel CAD and Diabetes Mellitus

Author	Type of Study and Years of Recruitment	Number of Patients PCI/CABG	Primary Endpoint for PCI and CABG	Comments
SYNTAX (92,93) 20079596 23413014	Randomized 2005-2007	Overall 903/897 DM 231/221	DM: 12-mo death, stroke, MI, or revasc: 26.0% vs. 14.2% (HR: 1.83; 95% CI: 1.22-1.73; p=0.003) DM: 5-y death, stroke, MI, or revasc: 46.5% vs. 29.0% (HR: 1.81; 95% CI 1.31-2.48; p<0.001) DM: 5-y death, stroke, MI: 23.9% vs. 19.1% (HR: 1.27; 95% CI 0.84-1.92; p=0.065)	Criterion for noninferiority of PCI to CABG was not met in overall study. Criterion for noninferiority of PCI to CABG was not met in overall study.
CARDia (87) 20117456	Randomized 2002-2007	DM 256/254	DM: 1-y death, stroke, or MI: 13.0% vs. 10.5% (OR: 1.25; 95% CI: 0.75-2.09; p=0.39)	Criterion for noninferiority of PCI to CABG was not met.
BARI 2D (76) 19502645	Prestratified/randomized to revasc-medical therapy, 2001-2005	DM 798/807	Death from any cause: • Medical: 87.8% • Revasc: 88.3% • p=0.97	5-y freedom from death, MI, repeat revasc: PCI vs. medical (77.0% vs. 78.9; p=0.15) CABG vs. medical (77.6% vs. 69.5%; p=0.01) Interaction p=0.002
ARTS I (85,94,95) 11479249 11297702 16098418	Randomized 1997-1998	Overall 600/605 DM 112/96	Overall: 5-y composite endpoint of death, stroke, or MI 18.2% vs. 14.9% (RR: 1.22; 95% CI: 0.95-1.58; p=0.14) DM: 1-y freedom from death, stroke, MI, or revasc (63.4% vs. 84.4%; p< 0.001)	N/A
MASS II (74) 17184637	Randomized 1995-2000	Overall 205/203 DM 56/59	DM: 1-y death 5.3% vs. 6.8% (p=0.5)	N/A
FREEDOM (91) 18215589	Randomized 2005-2010	DM 953/947	DM: 5-y death: 16.3% vs. 10.9%; p=0.049 DM: 5-y primary composite endpoint of death, nonfatal MI, or nonfatal stroke (26.6% vs. 18.7%; p=0.005)	N/A

ARTS indicates Arterial Revascularization Therapies Study; BARI 2D, Bypass Angioplasty Revascularization Investigation 2 Diabetes; CABG, coronary artery bypass graft; CAD, coronary artery disease; CARDia, Coronary Artery Revascularization in Diabetes; CI, confidence interval; DM, diabetes mellitus; FREEDOM, Future Revascularization Evaluation in Patients with Diabetes Mellitus: Optimal Management of Multivessel Disease; HR, hazard ratio; MASS II, Medicine, Angioplasty, or Surgery Study II; MI, myocardial infarction; mo, month(s); OR, odds ratio; PCI, percutaneous coronary intervention; revasc, revascularization; RR, relative risk; SYNTAX, Synergy Between Percutaneous Coronary Intervention with TAXUS and Cardiac Surgery; and y, year(s).

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