Best of the ACC 2010 Scientific Session

Highlights From the 59th Annual American College of Cardiology Scientific Session, March 14-16, 2010, Atlanta, GA

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Key words: MitraClip® • Heart failure • Type 2 diabetes mellitus • Acute coronary syndrome • Hypertension

This year's meeting of the American College of Cardiology presented important new data on many topics. Discussed here are key studies on mitral valve repair, the comparison of primary catheter ablation versus drug therapy for recurrent atrial fibrillation (AF), the combination of fibrate and statin therapy and cardiovascular disease (CVD) outcomes in patients with type 2 diabetes (T2DM), along with other important investigations.

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The EVEREST II Study

The Endovascular Valve Edge-to-Edge Repair (EVEREST II) study[1] evaluated the safety and effectiveness of the MitraClip® (Abbott Laboratories, Abbott Park, IL) procedure system as compared with open-chest surgery in patients with mitral insufficiency (Figure 1).

A total of 279 patients who met the American College of Cardiology/American Heart Association guidelines for mitral valve surgery (moderate-to-severe [Grade 3+] or severe [Grade 4+] mitral regurgitation), were randomly assigned to a 2:1 ratio to treatment with the MitraClip device (184 patients) or mitral valve repair or replacement surgery (95 patients) to determine if percutaneous mitral valve repair would be noninferior with regard to effectiveness and superior with regard to safety compared with mitral valve surgery. Patients included in the study if symptomatic had left ventricular ejection fraction (LVEF) > 25% and LV end-systolic dimension < 56 mm and if asymptomatic with 1 or more of the following: LVEF 25% to 60%, LV end-systolic dimension > 39 mm, new-onset atrial fibrillation, or pulmonary hypertension. Patients were excluded if they had suffered a myocardial infarction (MI) within 12 weeks, were in need of other cardiac surgery, had a serum creatinine > 2.5 mg/dL, or had endocarditis or rheumatic heart disease. Mitral valve anatomical exclusions included a mitral valve area < 4 cm^2, leaflet flail width (> 14 mm) and gap (> 9 mm), or leaflet tethering/coaptation depth (> 11 mm) and length (< 2 mm). The baseline patient characteristics are depicted in Table 1.

The primary effectiveness endpoint was freedom from death, surgery for mitral valve dysfunction, and > 2+ mitral regurgitation at 12 months. The primary safety endpoint included death, MI, reoperation

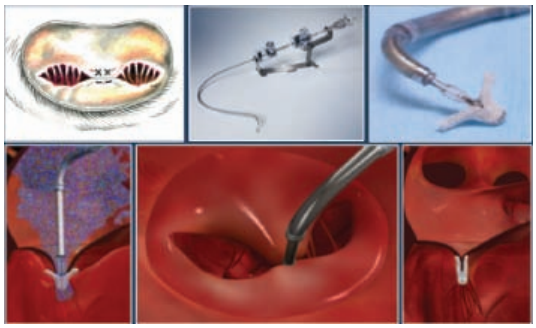

Figure 1. *The MitraClip® system (Abbott Laboratories, Abbott Park, IL). Adapted with permission from Cardiosource.*

Table 1
EVEREST II Randomized Clinical Trial
Demographic Comparison

	EVEREST II RCT	2008 STS Database		Isolated 1st Elective Operation for MR
	n = 279	Repair	Replace	High Volume Hospitals (> 140/y)
Age y (mean)	68	60	61	59
≥65 y	58%	37%	45%	n/a
≥75 y	32%	n/a	n/a	0%
NYHA Class III or IV	50%	26%	45%	n/a
CHF	86%	41%	58%	n/a
Hypertension	75%	60%	67%	43%
Diabetes mellitus	9%	13%	23%	6.5%
COPD/chronic lung disease	15%	17%	29%	n/a
EF (mean)	60%	53%	55%	56%

Baseline demographic characteristics of the patients in the Endovascular Valve Edge-to-Edge Repair (EVEREST II) study.
CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; EF, ejection fraction; EVEREST, Endovascular Valve Edge-to-Edge Repair study; MR, mitral regurgitation; NYHA, New York Heart Association; RCT, randomized controlled trial; STS, Society of Thoracic Surgeons.
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for failed surgical repair/replacement, nonelective cardiovascular (CV) surgery for adverse events, stroke, renal failure, deep wound infection, ventilation for > 48 hours, gastrointestinal complication requiring surgery, new-onset atrial fibrillation, sepsis, and transfusion of ≥2 U of whole blood. Secondary quality-of-life endpoints included New York Heart Association (NYHA) functional class and quality of life.

The MitraClip procedure was successful in 137 patients; 79 patients were available for 30-day follow-up. In the per-protocol analysis, 41 patients in the clip group did not achieve procedural success and were not analyzed further. Major adverse events at 30 days occurred in 9.6% of the clip group versus 57% of the control group ($P < .0001$ for superiority). This outcome was driven by increased need for blood transfusions in the control group. Clinical success rate at 12 months was 72% versus 88% ($P = .0012$ for noninferiority) in device and control groups, respectively (Figure 2).

In the intention-to-treat analysis, major adverse events at 30 days occurred in 15% of the clip group versus 48% of the control group ($P < .0001$ for superiority). Clinical success rate at 12 months was 67% versus 74% ($P = .0005$ for noninferiority), respectively. In the per-protocol group, 82% achieved 2+ or less mitral regurgitation with the MitraClip versus 97% in the control group at 12 months (Figure 3).

NYHA functional class I or II at follow-up was 98% in the clip group versus 88% in the control group (Figure 4). The improvement in the severity of mitral regurgitation and clinical improvement were associated with positive remodeling of the left ventricle with decompression of the left ventricle leading to significant reductions in LV end-diastolic volumes (Figure 4).

At 12 months, both groups reported significant improvement of residual mitral insufficiency, heart failure (HF) symptoms, LV dimensions, and quality of life. The MitraClip device has demonstrated both safety and clinical effectiveness and would be anticipated to represent a major advance in how cardiologists will approach patients with significant mitral insufficiency.

The ACCORD Lipid Trial

The Action to Control Cardiovascular Risk in Diabetes (ACCORD) Lipid trial[2] randomized adults with T2DM at an increased risk for CVD to determine whether fibrate and statin therapy improve CVD outcome as compared with statin therapy alone. In all, 5518 patients with T2DM and either pre-existing CVD or at least 2 additional CV risk factors were randomly assigned to treatment with simvastatin plus fenofibrate or to simvastatin plus placebo. Patients studied included those with T2DM with a hemoglobin A_{1c} level ≥ 7.5%,

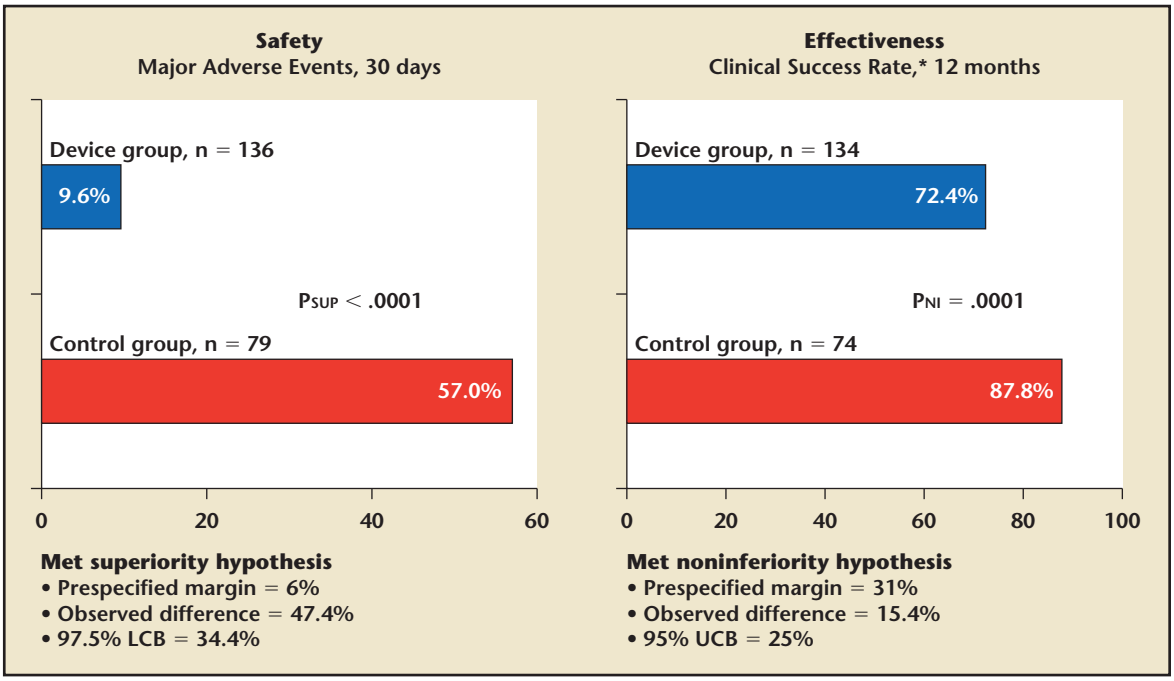


Figure 2. *Primary safety and effectiveness endpoints of the Endovascular Valve Edge-to-Edge Repair (EVEREST II) study. *Freedom from the combined outcome of death, MV surgery, or reoperation for MV dysfunction, MR > 2+ at 12 months. LCB, lower confidence bound; MR, mitral regurgitation; MV, mitral valve; UCB, upper confidence bound. Adapted with permission from Cardiosource.*

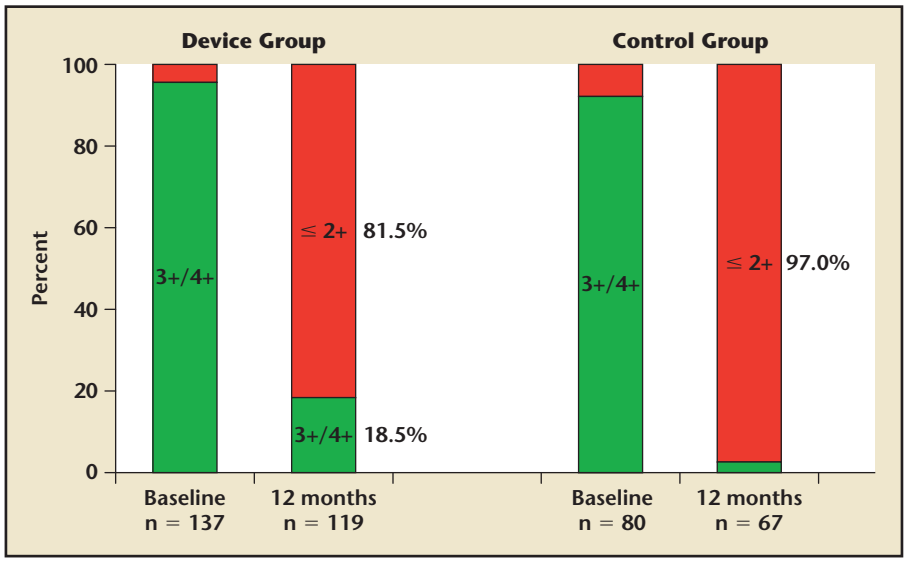


Figure 3. *Mitral regurgitation (MR) reduction with the MitraClip® system (Abbott Laboratories, Abbott Park, IL) and surgical treatment. Adapted with permission from Cardiosource.*

aged 40 to 79 years with clinical CVD or aged 55 to 79 years with subclinical CVD or at least 2 additional CV risk factors, low-density lipoprotein (LDL) cholesterol level between 60 and 180 mg/dL, high-density lipoprotein (HDL) cholesterol < 55 mg/dL for women and black patients or < 50 mg/dL for all others, and those with a triglyceride level < 750 mg/dL if not on lipid therapy or < 400 mg/dL if on lipid therapy.

The primary outcome was the first occurrence of a major CV event, including nonfatal heart attack, nonfatal stroke, or CVD death with secondary outcomes consisting of the primary outcome and revascularization or hospitalization for congestive heart failure (HF), major coronary disease event, nonfatal MI, stroke, death, or fatal or nonfatal congestive HF (Figure 5).

After a mean follow-up of 4.7 years, combination therapy did not significantly reduce combined rates of CVD, nonfatal heart attack, or nonfatal stroke as compared with simvastatin treatment alone ($P = .32$). There were no significant treatment

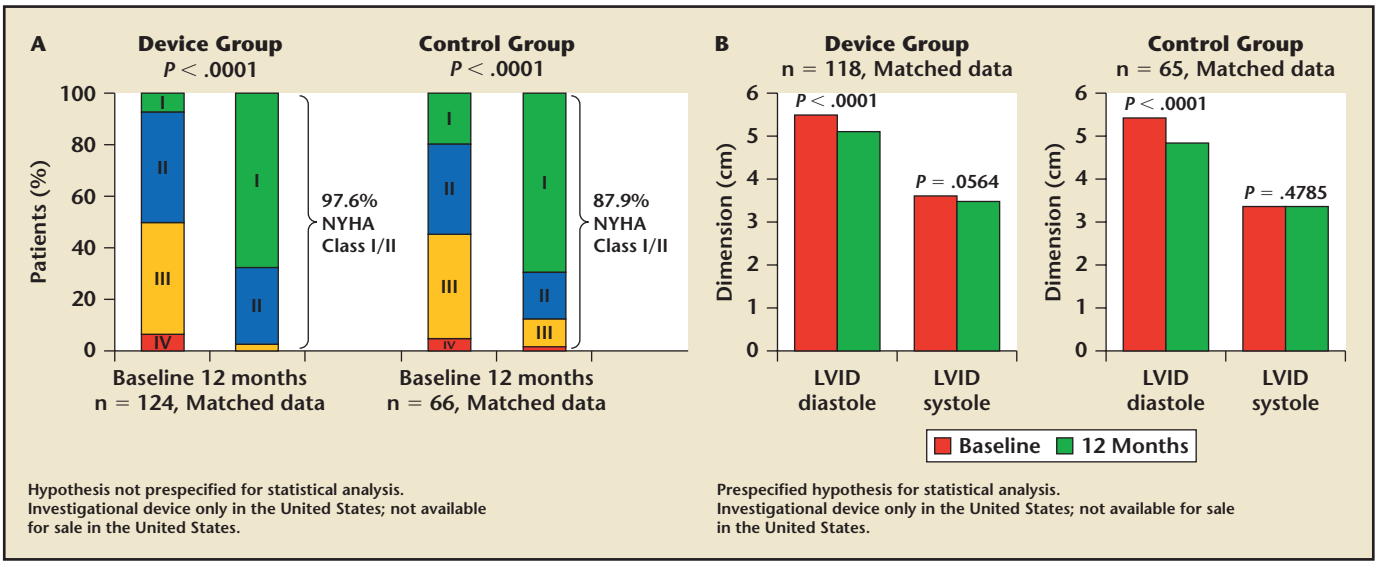


Figure 4. A) *Impact of MitraClip® system (Abbott Laboratories, Abbott Park, IL) on resulting functional class at baseline and after 12 months. EVEREST, Endovascular Valve Edge-to-Edge Repair study. Adapted with permission from Cardiosource.* **B)** *Impact of MitraClip® system (Abbott Laboratories, Abbott Park, IL) and surgery on left ventricular dimension. EVEREST, Endovascular Valve Edge-to-Edge Repair study. Adapted with permission from Cardiosource.*

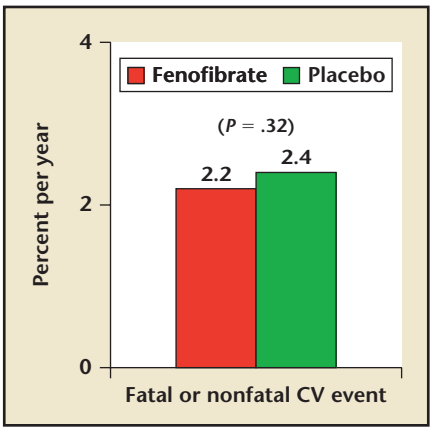


Figure 5. *Primary outcome of the ACCORD Lipid trial. ACCORD, Action to Control Cardiovascular Risk in Diabetes; CHF, congestive heart failure; CV, cardiovascular. Adapted with permission from Cardiosource.*

differences for any of the secondary outcome measures with an annual mortality rate of 1.5% in the fenofibrate-treated group and 1.6% in the placebo-treated group. Post-hoc subgroup analysis did suggest some heterogeneity in response to therapy, such as in patients who began the study with the highest triglyceride levels and lowest HDL cholesterol levels, possible benefit from combination therapy, and possible harm of combination therapy to women in the study but not to men.

The ACCORD BP Trial

The purpose of the Action to Control Cardiovascular Risk in Diabetes (ACCORD) BP trial[3] was to assess CV risk reduction in high-risk adults with T2DM when systolic blood pressure (SBP) is maintained below 120 mm Hg. A total of 4733 patients with T2DM, hypertension, and either preexisting CVD or a high risk for developing CVD were randomly assigned to a target SBP of either < 120 mm Hg or < 140 mm Hg. Patients with T2DM with an HbA_1C level ≥ 7.5%, aged 40 to 79 years with clinical CVD or aged 55 to 79 years with subclinical CVD or at least 2 additional CV risk factors and SBP 130-180 mm Hg on up to 1 antihypertensive medication, 130 to 170 mm Hg on 2 medications, or 130 to 160 mm Hg on 3 medications were included in the study. Patients with a serum creatinine level > 1.5 mg/dL or significant proteinuria were excluded from the trial. The mean estimated glomerular filtration rate of the study population was 92 mL/min/1.73 m^2. A variety of blood-pressure-lowering medication combinations were used to achieve the study blood pressure goals. The primary endpoint consisted of a composite of the following events: combined rate for a major CVD event such as nonfatal MI, nonfatal stroke, or CV death. Secondary endpoints included total mortality, CV deaths, nonfatal MI, nonfatal stroke, and total stroke.

The SBP averaged 119 mm Hg in the intensive therapy group and 134 mm Hg in the standard therapy group. There was no significant difference between the 2 groups in the combined rate of nonfatal heart attack or stroke, or CV death (P = .20) after an average of 4.7 years of follow-up (Table 2). Stroke risk was significantly lower with intensive therapy (0.3% vs 0.5%; P = .01). There was a reduction in the development of microalbuminuria and the urinary albumin-to-creatinine ratio in the aggressively treated arm.

Table 2
Primary and Secondary Outcomes

	Intensive Events (%/y)	Standard Events (%/y)	HR (95% CI)	*P*
Primary	208 (1.87)	237 (2.09)	0.88 (0.73-1.06)	.20
Total mortality	150 (1.28)	144 (1.19)	1.07 (0.85-1.35)	.55
Cardiovascular deaths	60 (0.52)	58 (0.49)	1.06 (0.74-1.52)	.74
Nonfatal MI	126 (1.13)	146 (1.28)	0.87 (0.68-1.10)	.25
Nonfatal stroke	34 (0.30)	55 (0.47)	0.63 (0.41-0.96)	.03
Total stroke	36 (0.32)	62 (0.53)	0.59 (0.39-0.89)	.01

Outcomes of the ACCORD BP trial. Also examined fatal/nonfatal HF (HR = 0.94, $P = 0.67$), a composite of fatal coronary events, nonfatal MI, and unstable angina (HR = 0.94, $P = 0.50$) and a composite of the primary outcome, revascularization, and unstable angina (HR = 0.95, $P = 0.40$).
ACCORD, Action to Control Cardiovascular Risk in Diabetes; BP, blood pressure; CI, confidence interval; HF, heart failure; HR, hazard ratio; MI, myocardial infarction.
Adapted with permission from Cardiosource.

The investigators concluded that the study does not support the reduction of CV risk by achieving SBP goals < 120 mm Hg in high-risk patients with T2DM. There was a higher risk of significant adverse events such as syncope and hyperkalemia, and small elevations in serum creatinine in the intensive blood pressure control group, but also a 41% lower stroke rate. The lack of a broader reduction of CV events in this study may be surprising. Whether this is related to excluding patients with significant chronic kidney disease (diabetic and hypertensive nephropathy) who would be at higher risk of CVD events is important before generalizing these results to the broader patient population of diabetic patients with hypertension that may represent the majority of patients cared for in "real world" clinical settings.

The NAVIGATOR Trial

The Nateglinide And Valsartan in Impaired Glucose Tolerance Outcomes Research (NAVIGATOR) trial[4] was designed to determine whether the risk of diabetes and CV events could be reduced in patients with impaired glucose tolerance (IGT). This was a prospective, multinational, randomized, double-blind, placebo-controlled trial with 9306 patients with IGT who were either older than age 50 years with diagnosed CVD or older than age 55 years with at least 1 risk factor for CVD. Patients with IGT had fasting glucose levels between 95 and 125 mg/dL. Patients were excluded if they had any laboratory abnormality or condition that could interfere with the assessment of drug efficacy and safety, used an angiotensin-converting enzyme (ACE) inhibitor or angiotensin receptor blocker (ARB) for hypertension, or used any antidiabetic medication within the last 5 years. Study patients' baseline characteristics are shown in Table 3.

Treatment was either a postprandial glucose-lowering drug (nateglinide therapy, up to 60 mg 3 times daily before meals) or an ARB (valsartan, up to 160 mg once daily) or both. There were co-primary endpoints, including the development of diabetes; a core CV outcome composite of death from CV causes, nonfatal MI, nonfatal stroke, or hospitalization for HF; and composite of individual components,

Table 3
Baseline Patient Characteristics

	Nateglinide n = 4645	Placebo n = 4661
Glycemic indices		
Fasting plasma glucose (mmol/L)	6.1 ± 0.45	6.1 ± 0.46
2-hour plasma glucose (mmol/L)	9.2 ± 0.93	9.2 ± 0.94
Glycated hemoglobin (%)	5.8 ± 0.45	5.8 ± 0.48
Metabolic syndrome, n (%)	3896 (83.9)	3898 (83.6)
Lipids		
Total cholesterol, mg/dL	210 ± 41	210 ± 43
HDL, mg/dL	50 ± 13	50 ± 13
LDL, mg/dL	126 ± 36	127 ± 38
Triglycerides, mg/dL	151 (109, 208)	150 (107, 209)
Creatinine, mg/dL	0.9 ± 0.2	0.9 ± 0.2
Estimated GFR mL/min/1.73 m^2	80.3 ± 18.6	81.1 ± 19.0
Urinary albumin:creatinine (mg/g)	7.1 (4.5, 14.1)	7.1 (4.5, 14.8)

Baseline characteristics of patients in the NAVIGATOR trial.
GFR, glomerular filtration rate; HDL, high-density lipoprotein; LDL, low-density lipoprotein; NAVIGATOR, Nateglinide And Valsartan in Impaired Glucose Tolerance Outcomes Research Trial.
Adapted with permission from Cardiosource.

hospitalization for unstable angina, or arterial revascularization.

With regard to the effect of valsartan, at a mean follow-up of 5 years, incident diabetes occurred in 33% of the valsartan-treated group versus 37% of the placebo-treated group ($P < .001$). There was no difference in the extended CV outcome (15% vs 15%; P = NS) or core CV outcome (8.1% vs 8.1%; P = NS).

With regard to the effect of nateglinide, incident diabetes occurred in 36% of the nateglinide-treated group versus 34% of the placebo-treated group ($P = .05$). The extended CV outcome (14% vs 15%; P = NS) and core CV outcomes (7.9% vs 8.3%; P = NS), were not different between nateglinide and placebo. Hypoglycemia occurred in 20% versus 11% ($P < .001$) and study drug discontinuation occurred in 11% versus 10% ($P = .23$), respectively. Among patients with IGT and CVD or CV risk factors, valsartan was effective at reducing incident diabetes; however, this did not translate into a reduction of long-term adverse CV events. Nateglinide reduced neither incident diabetes nor adverse CV events.

The RACE II Study: A Comparison Between Lenient Versus Strict Rate Control in Patients With HF

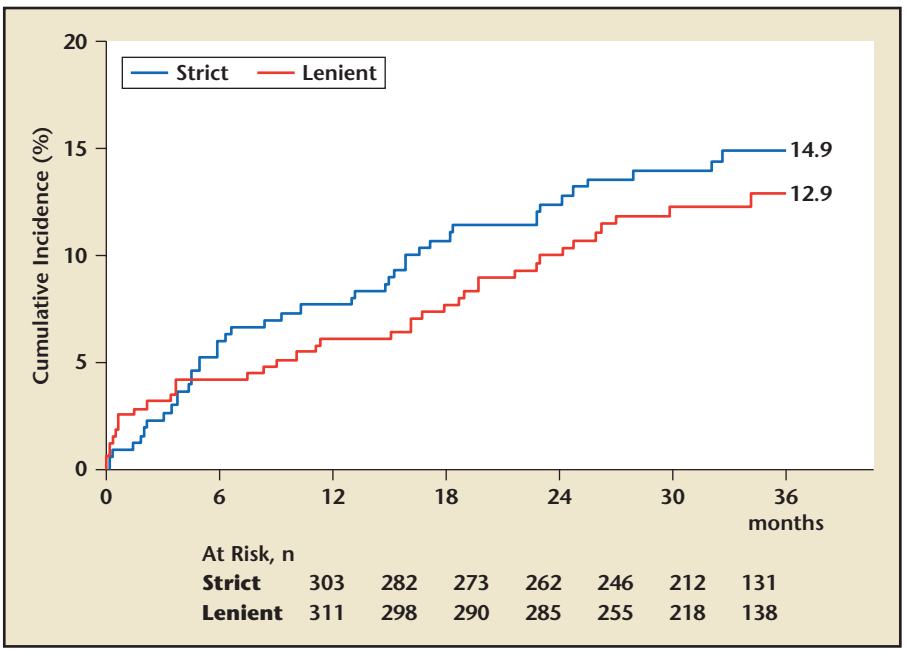
The Rate Control Efficacy in Permanent Atrial Fibrillation (RACE) II Study[5] compared a strategy of lenient (< 110 beats/min) versus strict (< 80 beats/min) rate control in patients with and without HF. A total of 614 patients were randomized to receive a rate control drug, which was adjusted to achieve resting heart rate goals (strict: < 80 beats/min at rest and < 110 beats/min at 25% duration of maximal exercise time and lenient: < 110 beats/min at rest) during follow-up visits at 1, 2, and 3 months, and annually. Rate control treatment included β-blockers, non–dihydropyridine calcium channel blockers, and digoxin alone or in combination. Patients included in this study had permanent atrial fibrillation (AF) for < 12 months, a resting heart rate > 80 beats/min, age < 81 years, and were on oral anticoagulation. Patients with paroxysmal AF, unstable HF, stroke, recent cardiac surgery, or current or foreseen pacemaker, implantable cardioverter defibrillator (ICD), or cardiac resynchronization therapy were excluded. The primary endpoints were time to a CVD event, including CV mortality, hospitalization for HF, systemic emboli, major bleeding, syncope, sustained ventricular tachycardia, cardiac arrest, pacemaker implant for bradycardia, and ICD implant for ventricular arrhythmias.

The estimated incidence of primary outcome for strict and lenient rate control was 14.9 and 12.9, respectively (Figure 6). Secondary endpoints (strict vs lenient) of death by any cause (18% vs 17%), symptoms emblematic of AF (46% vs 45.6%), and NYHA functional class I (23.4% vs 23.3%) were not different. The investigators concluded that lenient rate control was not inferior to strict rate control in patients with permanent AF.

The EXPLORE Xa Trial

The Randomized Clinical Trial of Three Doses of a Long-Acting Oral Direct Factor Xa Inhibitor Betrixaban in Patients With Atrial Fibrillation (EXPLORE Xa)[6] was a dose-finding and effectiveness trial assessing a strategy of factor Xa inhibition in reducing risk of AF-related stroke. In total, 508 patients were randomized 1:1:1:1 to receive Betrixaban (BTX; Portola Pharmaceuticals, South San Francisco, CA/Merck, Whitehouse Station, NJ) at 40 mg, 60 mg, or 80 mg once daily for 3 months or dose-adjusted warfarin. Inclusion criteria for this trial included those

Figure 6. *Primary event outcome of the Rate Control Efficacy in Permanent Atrial Fibrillation (RACE) II study. Adapted with permission from Cardiosource.*



with nonvalvular AF with at least 1 risk factor for stroke, no uncontrolled hypertension, taking ≤ 162 mg aspirin daily, an International Normalized Ratio (INR) ≤ 2.2 at randomization, or inability to comply with INR monitoring. Patients were excluded if they weighed < 40 kg, had hemodialysis within the past year, AF due to reversible cause, had a mechanical prosthetic valve, or a condition other than AF requiring anticoagulation, a SBP > 160 mm Hg, active endocarditis, scheduled major surgery or pulmonary vein isolation procedure, or had suffered a stroke, systemic embolic event, or acute coronary syndrome within 30 days. The mean $CHADS_2$ (congestive heart failure, hypertension, age, diabetes mellitus, stroke or transient ischemic attack) score was 2.2. The primary endpoint was the time to the occurrence of major or clinically relevant nonmajor bleeding with secondary endpoints including time to occurrence of any bleeding (major, clinically relevant nonmajor, and minimal) and time to occurrence of death, stroke, MI, or other systemic embolism.

The primary endpoint was less likely to occur at the 40-mg dose of BTX compared with the 60-mg or 80-mg dose and with warfarin (Figure 7). In fact, all doses of BTX resulted in less major or clinically relevant nonmajor bleeding than warfarin.

A strategy of inhibiting factor Xa with low-dose BTX is superior to warfarin at controlling bleeding in patients with AF. Further study will delineate the effectiveness of this agent in preventing stroke and bleeding in patients with AF.

The CABANA Pilot Study

The Catheter Ablation versus Antiarrhythmic Drug Therapy for Atrial Fibrillation (CABANA) Pilot Study[7] compared primary catheter ablation for the elimination of AF with state-of-the-art drug therapy for reducing recurrent AF in high-risk patients. This pilot study comprised advanced AF patients (n = 60) with multiple underlying CVD. In all, 31 patients were randomized to receive antiarrhythmic drug therapy or heart rate control drugs alone; 29 patients underwent isolation of all 4 pulmonary veins. In the medical management arm 16% received medical therapy to maintain sinus rhythm, 13% were treated for rate control only, and 71% were treated for both. To be eligible for the study, patients had to have documented ≥ 2 paroxysmal AF episodes (≥ 1 hour) over 4 months or ≥ 1 persistent AF episode (> 1 week), be age ≥ 65 years, or age < 65 years with ≥ 1 risk factor (hypertension, diabetes, HF, prior cerebrovascular accident or transient ischemic attack), left atrial size > 5.0 cm, ejection fraction ≤ 35%, and be eligible for ablation and currently taking ≥ 2 rhythm control or ≥ 3 rate control drugs.

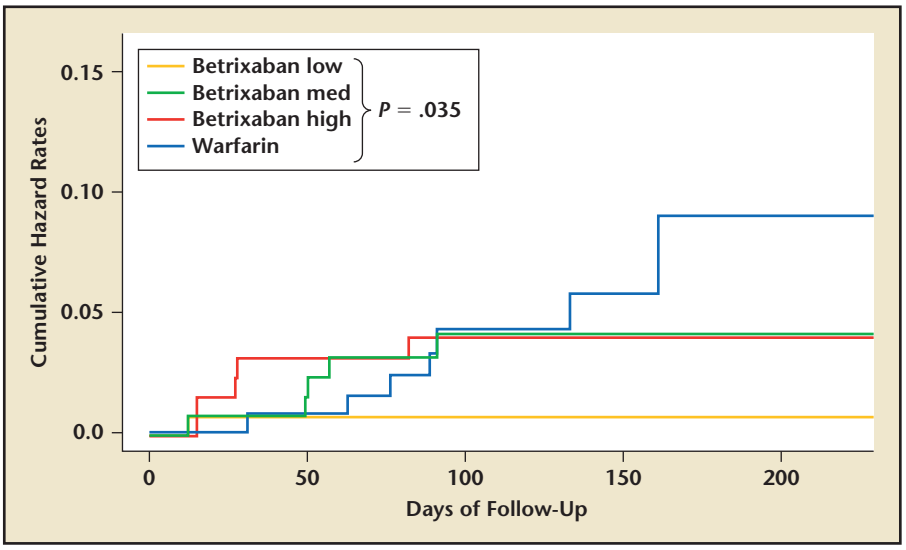


Figure 7. *Incidence of the primary endpoint of 3 doses of betrixaban compared with warfarin. Adapted with permission from Cardiosource.*

The primary endpoint was recurrence of AF. The incidence of freedom from symptomatic AF was significantly higher in the catheter ablation arm, as compared with the antiarrhythmic drug arm (65% vs 41%, hazard ratio [HR] 0.46; P = .03), whereas the incidence of any AF, atrial flutter, or atrial tachycardia was similar between the 2 arms (66% vs 72%, HR 0.69; P = .26). The results of the CABANA pilot study show that catheter ablation is associated with a reduction in symptomatic AF in high-risk patients as compared with medical therapy, although there was no difference in the incidence of any atrial arrhythmia. The results of the CABANA pivotal trial will shed more light on the comparison of ablation and medical therapy in patients with AF.

The DOSE Study

The Diuretic Optimization Strategies Evaluation (DOSE) study[8] was a randomized, double-blind, placebo-controlled trial comparing the safety and efficacy of high- versus low-dose intravenous (IV) furosemide treatment and separate dose versus continuous infusion in patients with acute decompensated heart failure (ADFH). Patients included in this

study had a prior clinical diagnosis of HF with daily home use of an oral loop diuretic for at least 1 month, daily oral dose of furosemide between 80 and 240 mg (or equivalent), HF defined by at least 1 symptom and 1 sign, and anticipated need for IV loop diuretics for at least 48 hours; they were excluded if they received or planned to receive IV vasoactive treatment (inotropes, vasodilators) or ultrafiltration therapy for HF, had SBP < 90 mm Hg, serum creatinine level > 3.0 mg/dL at baseline or renal replacement therapy, had B-type natriuretic peptide (BNP) < 250 ng/mL or N-terminal proBNP < 1000 mg/mL, had an acute coronary syndrome within 4 weeks or anticipated need for coronary angiography or other procedures requiring IV contrast. Within 24 hours of admission, 308 patients were assigned to 1 of 4 treatment arms for 72 hours: continuous IV high-dose (2.5 × baseline oral dose) furosemide; continuous IV low-dose (1 × oral dose) furosemide; IV bolus high-dose furosemide every 12 hours; and IV bolus low-dose furosemide every 12 hours. The primary efficacy endpoint was the Patient Global Assessment by visual analog scale (VAS) and the primary safety endpoint was change in serum creatinine from baseline to 72 hours. There was no difference between every 12-hour dosing and continuous infusion of furosemide on the VAS area under the curve (AUC) (Figure 8).

There was no significant difference in change in serum creatinine (0.05 vs 0.07 mg/dL; $P = .45$). Secondary endpoints such as net volume loss (4237 vs 4249 mL; $P = .89$), % treatment failure (38% vs 39%; $P = .88$), change in weight at 72 hours (−6.8 vs 8.1 lbs; $P = .20$), dyspnea VAS AUC at 72 hours (4456 vs 4699; $P = .36$), and length of stay (5 vs 5 days; $P = 0.97$) were similar between the 2 groups. For the low and high intensification of furosemide dosing analysis, there was no difference on the VAS or change in creatinine from baseline (0.04 vs 0.08 mg/dL; $P = .21$). Secondary endpoints such as net volume loss (3575 vs. 4899 mL; $P = 0.001$), change in weight at 72 hours (−6.1 vs 8.7 lbs; $P = 0.011$), and dyspnea VAS at 72 hours were significantly better in the high-dose furosemide group.

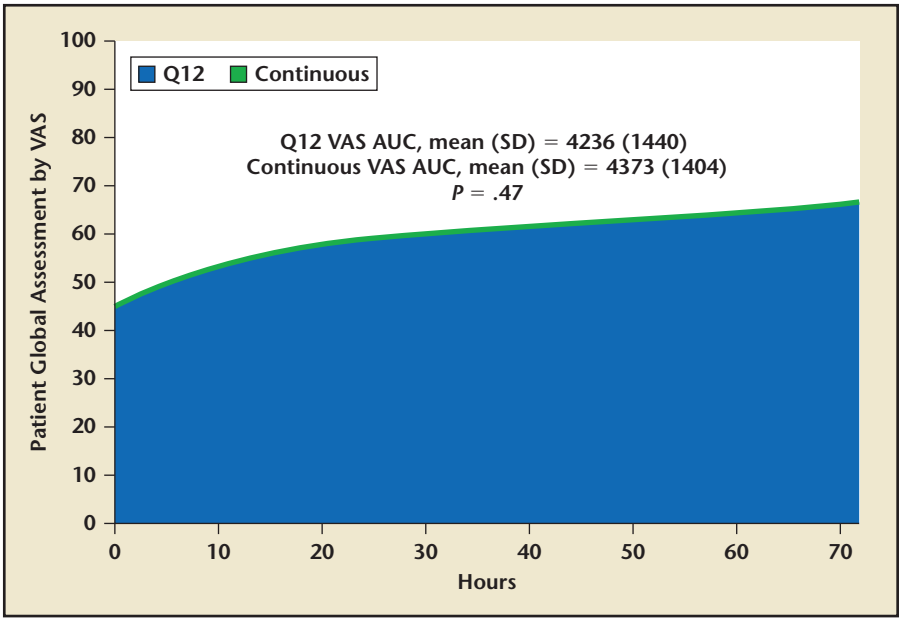


Figure 8. *Primary endpoint of the Diuretic Optimization Strategies Evaluation (DOSE) trial. VAS AUC, area under the visual analog scale; Q12, every 12 hours; SD, standard deviation. Adapted with permission from Cardiosource.*

The results of the DOSE trial will have important implications in how diuretic treatment is applied to patients with ADHF. DOSE showed no benefit from continuous infusion over regular pulse dosing. However, the high intensification dose of furosemide was associated with a significant improvement in net diuresis, weight loss, and symptom relief, as compared with the low intensification dose. Changes in creatinine noted in the high intensification arm were transient.

The ASPIRE Trial

The Effect of the Direct Renin Inhibitor Aliskiren on Left Ventricular Remodeling Following Myocardial Infarction with Left Ventricular Dysfunction (ASPIRE) trial[9] evaluated the effect of additional blockade of the renin-angiotensin-aldosterone system with the addition of the direct renin inhibitor aliskiren to conventional therapy, including ACE inhibitors, ARBs, and LV remodeling, on post-MI patients. A total of 802 patients 2 to 6 weeks after MI with LV dysfunction were treated with aliskiren titrated to 300 mg/d.

The primary endpoint of LV end-systolic volume as assessed by echocardiography decreased by 4.4 mL in the aliskiren-treated group and 3.5 mL in those treated with placebo. The investigators concluded that the addition of aliskiren to conventional post-MI treatments was not beneficial and did not affect LV function or size. There was a potential for more adverse events

including hyperkalemia, hypotension, and renal dysfunction in the patients treated with aliskiren.

The STICH Trial

The Influence of Reduction of Left Ventricular Volume on Outcome After Coronary Artery Bypass Grafting With or Without Surgical Ventricular Reconstruction (STICH) trial[10] evaluated whether coronary artery bypass grafting (CABG) with surgical ventricular reconstruction (SVR) in patients with anterior-apical regional LV dysfunction would be superior to CABG alone in reducing death and cardiac hospitalization and improving quality of life. The primary endpoint was death plus long-term survival free of cardiac hospitalization. Though a greater reduction in LV end-systolic volume index was observed in the CABG + SVR group, there was no significant difference in the primary endpoint of death and cardiac hospitalization (58% vs 59%; $P = .90$) or improvement in the secondary endpoints including NYHA HF classification or Canadian Cardiovascular Society angina classification with CABG + SVR over CABG alone.

The JETSTENT Trial

The Randomized Comparison of AngioJet Rheolytic Thrombectomy Before Direct Infarct Artery Stenting to Direct Stenting Alone in Patients with Acute Myocardial Infarction (JETSTENT) trial[11] was designed to determine if rheolytic thrombectomy would improve myocardial reperfusion and clinical outcomes for patients with acute ST-segment elevation MI (STEMI). Macro- and microembolization are known to occur commonly during percutaneous coronary intervention in STEMI. At times this can lead to the obstruction of the microvasculature and delay or prevent cellular reperfusion, leading to worse outcomes. A total of 501 patients were enrolled from 8 sites in Europe and South America.

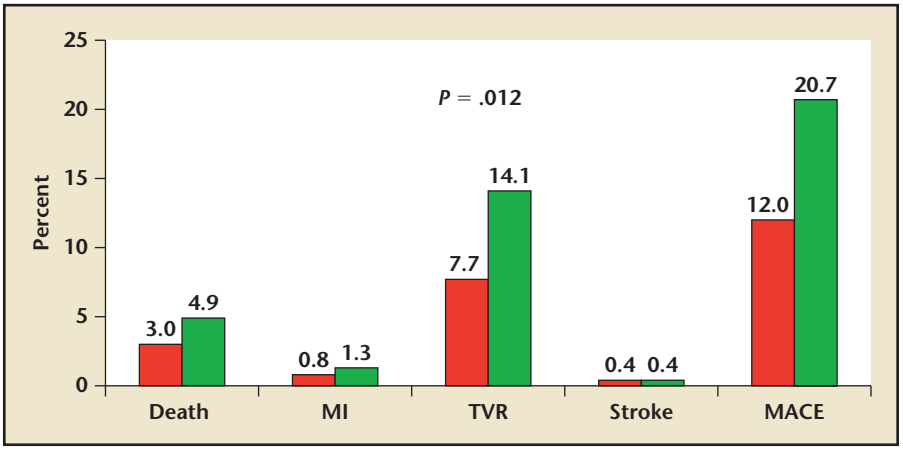


Figure 9. *Primary endpoint of Randomized Comparison of AngioJet Rheolytic Thrombectomy Before Direct Infarct Artery Stenting to Direct Stenting Alone in Patients with Acute Myocardial Infarction (JETSTENT) trial. MACE, major adverse cardiac events; MI, myocardial infarction; TVR, target vessel revascularization. Adapted with permission from Cardiosource.*

The primary endpoints were > 50% reduction of ST-segment resolution at 30 minutes postprocedure, final infarct size at 30 days, major adverse cardiac events at 1, 6, and 12 months, and death, and for readmission for HF at 12 months. Rheolytic thrombectomy, in addition to direct stenting, produced more rapid resolution of the ST-segment elevation than stenting alone without any change in infarct size. The incidence of major adverse cardiac events was significantly lower in the group receiving rheolytic thrombectomy at 6 months (Figure 9).

The PLATO Trial

Ticagrelor Versus Clopidogrel In Patients With Acute Coronary Syndromes Undergoing Coronary Artery Bypass Surgery (PLATO) trial[12] evaluated whether ticagrelor is more effective than clopidogrel in reducing the incidence of death from vascular causes, MI, or stroke, without increasing the overall rate of major bleeding in patients undergoing CABG within 7 days of their last intake of the study drug.

This study was a retrospective, postrandomized evaluation of 1261 patients who underwent CABG and were given either ticagrelor or clopidogrel. The primary composite endpoint of CV death, heart attack, and stroke showed no difference, although the total mortality rate was lower in ticagrelor-treated patients (4.6% vs 9.2%) (Figure 10). The secondary endpoint of CABG-related major bleeding was no different (Figure 10).

Ticagrelor was similar to clopidogrel in terms of the composite primary endpoint though there was a significant reduction in all-cause and CV mortality without any reduction in MI or stroke. This mortality benefit was observed within 1 month of the index CABG procedure. There are serious limitations to this analysis, including the fact that it was performed in a nonrandomized fashion and there was lack of full characterization of the causes of post-CABG mortality. Interestingly,

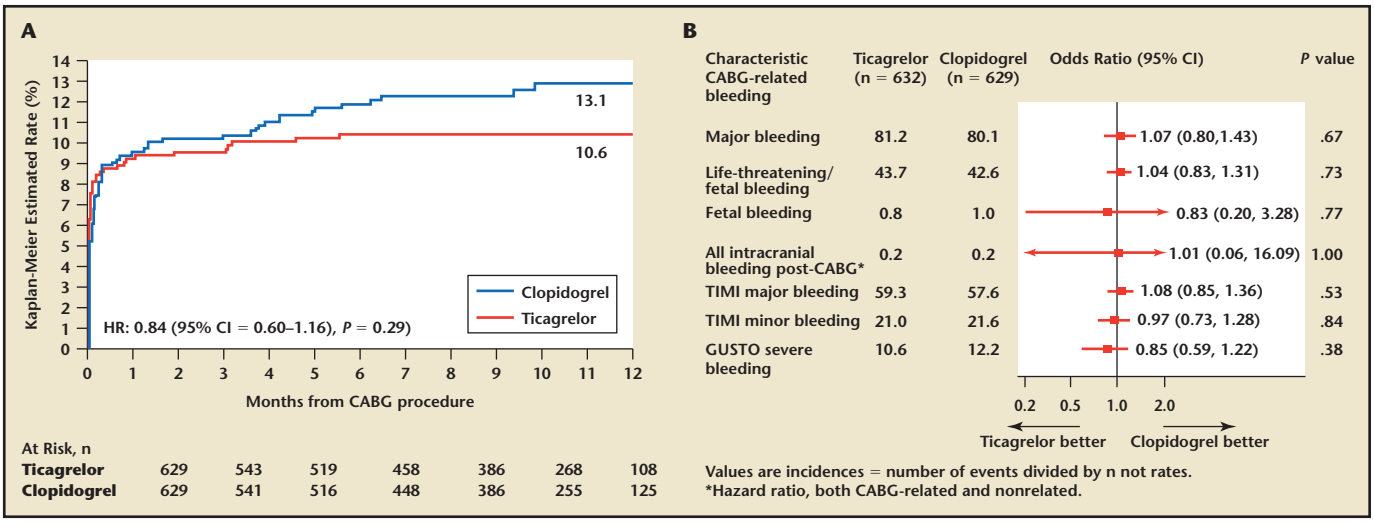


Figure 10. A) *Primary endpoint of Ticagrelor Versus Clopidogrel In Patients With Acute Coronary Syndromes Undergoing Coronary Artery Bypass Surgery (PLATO) study. CABG, coronary artery bypass graft; CI, confidence interval; CV, cardiovascular; HR, hazard ratio; MI, myocardial infarction. Adapted with permission from Cardiosource.* **B)** *Bleeding endpoint of Ticagrelor Versus Clopidogrel In Patients With Acute Coronary Syndromes Undergoing Coronary Artery Bypass Surgery (PLATO) study. CABG, coronary artery bypass graft; GUSTO, Global Strategies for Opening Occluded Coronary Arteries; TIMI, thrombolysis in myocardial infarction. Adapted with permission from Cardiosource.*

there was no reduction in bleeding events with ticagrelor compared with clopidogrel. ■

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Main Points

- In patients with severe mitral insufficiency, repair with the MitraClip system (Abbott Laboratories, Abbott Park, IL) was possible. This therapy demonstrated improved safety at 30 days compared with surgery, primarily by reducing the need for blood transfusion. At 30 days, major adverse events occurred in 9.6% of the clip group as compared with 57% in the control group.
- The Rate Control Efficacy in Permanent Atrial Fibrillation (RACE) II study showed that lenient rate control is not inferior to strict rate control in patients with permanent atrial fibrillation (AF). In fact, it is more convenient because it requires fewer outpatient visits, fewer examinations, and lower doses of medication. Lenient rate control can be used in both high- and low-risk patients with AF.
- Although surgical ventricular reconstruction (SVR) was demonstrated to reduce left ventricular end-systolic volume to a greater extent than coronary artery bypass grafting (CABG) alone, this result did not translate into an improvement in cardiovascular morbidity or mortality in the Surgical Treatments for Ischemic Heart Failure Hypothesis (STICH) trial. Based on these results, routine SVR at the time of CABG is not recommended at this time.

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