Late-Breaking Clinical Trial Abstracts and Clinical Science: Special Reports Abstracts From the American Heart Association’s Scientific Sessions 2010

Hot Topics Abstracts From the Resuscitation Science Symposium 2010

American Heart Association
Learn and Live

TWO-DAY EVENT
RESUSCITATION SCIENCE SYMPOSIUM
Nov. 13–Nov. 14

FOUR-DAY EVENT
with SCIENTIFIC SESSIONS
Nov. 13–Nov. 16
Improved outcomes with ventricular assist devices have been demonstrated in continuous flow pumps utilizing axial flow technology compared to older pulsatile designs. The study endpoint is a composite of all cause mortality and adjudicated HF hospitalization (defined as an ICD with CRT in a 1:1 ratio in addition to optimal heart failure medical therapy. The primary control group. Follow-up of 2%, crossover of 5% and 7% and a projected annual event rate of 11% in the study was designed to achieve 85% power to detect a 25% relative risk reduction in the noninferior to that of a contemporaneous control group undergoing bridge to transplant (BTT) with commercially available left ventricular assist devices and enrolled in the INTERMACS Registry. The noninferiority margin will be 15%, the trial design sample size provides >90% power to test the primary hypothesis at the one-sided 0.05 significance level. Results: 140 adults (28.8F, 72M; 43% ischemic) listed for transplant as UNOS status 1A or 1B, with BSA\(\geq1.2\) cm received HVADs as BTT at 30 sites. Baseline characteristics for HVAD patients including 15.5 mmHg. Over 85% of patients were receiving one or more intravenous inotropes and 25% were supported with an IABP at HVAD implantation. Conclusions: The primary endpoint and survival will be compared between HVAD patients and contemporaneous control patients from INTERMACS. Adverse events, operative times and transfusion requirements will also be reviewed. In addition, we will present quality of life and functional outcomes for the HVAD patients. As the first FDA pivotal trial to incorporate a comparison against controls from the HVAD-sponsored INTERMACS Registry, ADVANCE’s novel design provides a model for investigation of future devices.

Author Disclosures: K.D. Aaronson: Research Grant; Modest; HeartWare, Terumo. Consultant/ Advisory Board; Modest; HeartWare. M.S. Slaughter: Research Grant; Modest; HeartWare. E. McGee: Consultant/Advisory Board; Modest; Thoratec. Consultant/Advisory Board; Significant; HeartWare. W.G. Gotts: None. M.A. Acker: Consultant/Advisory Board; Modest; Acorn, Thoratec, HeartWare. M.L. Jessup: Consultant/Advisory Board; Significant; HeartWare. L. Giovine: None. P. Loyalka: None. V. Jeewanandam: None. V. S. Healey, McMaster University, Hamilton, Canada; J. Malcolm O. Arnold, University of Toronto, Toronto, Canada. Consultant/Advisory Board; Modest; St. Jude Medical, V. Teuteberg: HeartWare, Thoratec, Terumo. A.S. Anderson: None. R.L. Kormos: None. J.J. Teuteberg: Speakers Bureau; Modest; Xdx. Consultant/Advisory Board; Modest; Thoratec, Xdx. F.D. Pagani: Research Grant; Modest; HeartWare, Terumo, Thoratec. Consultant/Advisory Board; Significant; HeartWare. S.Boyer: Ownership Interest; Significant; HeartWare. Consultant/ Advisory Board; Modest; HeartWare. D. Hathaway: Employment; Significant; HeartWare. Ownership Interest; Significant; HeartWare. L.W. Miller: Research Grant; Significant; HeartWare, Thoratec, Honoraria; Modest; HeartWare, Thoratec, M.A. Acker: Consultant/Advisory Board; Modest; Acorn Cardiovascular, Inc.

The Effect of Eplerenone versus Placebo on Cardiovascular Mortality or Heart Failure Hospitalization in Subjects With NYHA Class II Chronic Systolic Heart Failure. EMPHASIS-HF

Faiez Zannad, INSERM, CIC 9501 and 4U61, Univ of Nancy, Vandoeuvre les Nancy, France; McMurray J John, British Heart Foundation Cardiovascular Research Unit, Unv of Glasgow, Glasgow, United Kingdom; Drexler Helmut, Clinic of Cardiology and Angiology, Hannover Med Sch., Hannover, Germany; Krum Henry, Monash Univ, Ctr of Cardiovascular Rsch and Education in Therapeutics, Melbourne, Australia; Van Veerdusen J Dirk, Thorax Ctr, Groningen, Netherlands; Swedberg Karl, Sahlgrenska Academy, Unv of Gothenburg, Gothenburg, Sweden; Pitt Bertram; Unv of Michigan, Ann Arbor, MI

The effect of eplerenone versus placebo on cardiovascular mortality or heart failure hospitalization in subjects with NYHA class II chronic systolic heart failure. EMPHASIS-HF Purpose: In chronic heart failure (HF), aldosterone antagonists have been shown to improve survival in patients with low ejection fraction and moderate-to-severe symptoms (NYHA III and IV). Efficacy of these agents was also shown when they were administered to patients with left ventricular dysfunction and signs and symptoms of CHF early after acute myocardial infarction. It is not known whether the selective aldosterone antagonist eplerenone can improve outcomes in mildly symptomatic patients. The Eplerone in Mild Patients Hospitalization And Survival Study in Heart Failure (EMPHASIS-HF) was designed to evaluate the effect of eplerenone on mortality and morbidity in patients with chronic systolic HF in NYHA class II. Methods: A total of 2681 patients with ejection fraction <30% and estimated glomerular filtration rate >30 mL/min/1.73 m2 have been recruited. Patients were randomized 1:1 to double-blind eplerenone or placebo in addition to standard chronic HF therapy. Doses were adjusted from 25 mg every other day to 50 mg daily, depending on serum potassium. The primary endpoint is a composite of time to cardiovascular death or first hospital admission for worsening HF, whichever occurs first Results and Conclusions: EMPHASIS-HF has prematurely reached its primary endpoint according to the predefined stopping rules. Full results will be presented at the meeting.

Author Disclosures: F. Zannad; Consultant/Advisory Board; Significant; Pfizer, M.A. John; Pfizer. D. Helmut; None. K. Henry; Pfizer, V.J. Dirk; Pfizer, S. Karl; Pfizer, P. Bertram; Ownership Interest; Significant; electrolysis. Consultant/Advisory Board; Significant; Pfizer.
Acute Study of Clinical Effectiveness of Nesiritide in Decompensated Heart Failure Trial (ASCEND-HF)

Adrian F Hernandez, Christopher M O’Connor, Duke Clinical Rech Institute, Durham, NC; Randall C Starling, Cleveland Clinic, Cleveland, OH; Paul W Armstrong, Univ of Alberta, Edmonton, Canada; Kenneth Dickstein, Univ of Bergen, Bergen, Norway; Daniel Genovesio, Johnson & Johnson, Raritan, NJ; Vic Hasselblad, Gretchen M Heizer, Duke Clinical Rech Institute, Durham, NC; Michel Komajda, Univ Pierre Marie Curie, Paris, France; Barry Massie, Univ of California, San Francisco, San Francisco, CA; John J McMurray, Western Infirmary, Glasgow, Scotland, UK; Gerard de Moraes, Mollihat Hosp, Helsinki, Finland; Craig J Reist, Duke Clinical Rech Institute, Durham, NC; Jean L Rouleau, Montreal Heart Institute, Montreal, Canada; Karl Sweedberg, Sahlgrenska Academy, Goeteborg, Sweden; Robert M Califf, Duke Translational Medicine Institute, Durham, NC

Background. Nesiritide is a recombinant intravenous formulation of human B-type natriuretic peptide known to reduce dyspnea and intracardiac filling pressures within 3 hours of administration in patients with acute decompensated heart failure (ADHF). However, the effect of nesiritide on dyspnea at 6 or 24 hours is unknown. Moreover no clinical outcome trial exists that provides a reliable estimate of the effect of nesiritide on morbidity and mortality. Methods. In a prospective, double-blind randomized trial, ADHF patients within 24 hours of hospitalization were randomly assigned to receive either intravenous nesiritide or matching placebo for between 24 hours to 7 days. The 2 co-primary endpoints are (1) assessment of acute dyspnea at 6 or 24 hours, and (2) death or rehospitalization for HF within 30 days. Results. Enrollment will end in August, 2010 with the prespecified >7000 subjects from approximately 400 sites worldwide. Current baseline characteristics show that the median age is 68 years (25th/75th interquartile range [IQR]: 57 yrs-77yrs) and 34% of subjects are female. Ischemic heart disease is present in 60% and the median ejection fraction is 30% (25th/75th IQR: 20%, 37%): 32% have an ejection fraction <40%. Treatment pre-randomization included loop diuretics in 95.3%, inotropes in 4.4%, and vasodilators in 14.8%. A bolus of study drug was used in 61.3% of patients and the median duration of study drug infusion was 42.2 hours (25th/75th IQR: 24.1, 48.6 hrs). Last 30-day follow-up visit will occur in September, 2010. Conclusions. The data from the ASCEND-HF trial will evaluate whether nesiritide safely improves acute dyspnea at 6 or 24 hours as well as all-cause mortality and rehospitalization for heart failure at 30 days.

Late-Breaking Clinical Trials II

Hall B

Abstracts 21839–21752

Stroke Prevention Using the Oral Direct Factor Xa Inhibitor Rivaroxaban Compared With Warfarin in Patients With Nonvalvular Atrial Fibrillation (ROCKET AF)

Manesh R Patel for ROCKET AF Executive Steering Committee; Duke Univ, Durham, NC

Background. Anticoagulation with warfarin prevents ischemic stroke in patients with nonvalvular atrial fibrillation (AF), but routine coagulation monitoring, dose adjustments, and bleeding risk limit its overall use. The oral direct Factor Xa inhibitor rivaroxaban represents a potential alternative anticoagulant. Objective: To establish whether rivaroxaban is noninferior to dose-adjusted warfarin within a risk ratio margin of 1.46 for the prevention of all stroke and systemic embolic events. Methods: Patients with AF and a history of stroke or at least 2 stroke risk factors (n=14,269) were randomized at 1215 participating sites in 45 countries to receive either rivaroxaban, 20 mg, or dose-adjusted warfarin (target INR 2.5, range 2.0–3.0) double-blind. The primary efficacy endpoint was all adjudicated strokes (ischemic and hemorrhagic) and systemic embolic events. The primary analysis was based on establishing noninferiority in the per-protocol population. Results. These data are preliminary as final follow up and database closure is underway. The median patient age was 73 years; 40% were female, 63% had heart failure, 90% hypertension, 40% diabetes, and 55% a prior stroke or TIA. The intrinsic stroke risk of enrolled patients was high (15% had a CHADS2 score >3). The trial was stopped when the prespecified 0.05 protocol primary efficacy events had occurred. During the 5-year-patient-years of exposure (median 42 months), the INR on warfarin (mean 90) was within target range 16% of the time. At time of presentation, primary event rates, the absolute difference in primary event rates, all-cause mortality, rates of disabling or fatal stroke, hemorrhagic stroke and major bleeding will be reported. Conclusion: The ROCKET AF study will define the efficacy and safety of rivaroxaban as an alternative to warfarin for the prevention of stroke and systemic embolism in patients with nonvalvar AF.

Author Disclosures: M.R. Patel for ROCKET AF Executive Steering Committee: None.

Primary Results From the SMART AV Trial: A Randomized Trial Comparing Efficacy, Ecographic Guided and Algorithmic AV Delay Programming in Cardiac Resynchronization Therapy (CRT)

Kenneth A Ellenbogen, Med College of Virginia, Richmond, VA; Michael Gold, Med Univ of South Carolina, Charleston, SC; Bernd Lemke, Ruhr-University Bochum, Bochum, Germany; Ignacio Lozanno, Hosp Puerta de Hierro, Madrid, Spain; Timothy Meyer, Boston Scientific, St. Paul, MN; Sunnet Mittal, The St. Luke’s-Roosevelt Hosp Ctr, New York, NY; Jagmeet Singh, Massachusetts General Hospital, Harvard Med Sch, Boston, MA; Francis Spinale, Med Univ of South Carolina, Charleston, SC; Kenneth Stein, Boston Scientific, St. Paul, MN; Jennifer Van Eyk, Johns Hopkins Univ, Baltimore, MD; Alan Waggoner; Washington Univ Sch of Medicine, St. Louis, MO

Introduction: A number of small non-randomized studies have suggested optimization of the atrioventricular (AV) interval may improve response to CRT therapy. There are no large prospective randomized trials comparing the clinical and echocardiographic outcomes after AV interval optimization. Approximately 30% of patients who receive a CRT device experience a limitation in heart failure control and/or recurrent hospitalization due to LV (left ventricular) remodeling. One variable that may influence response can be the programmed AV delay. The SMART AV Trial prospectively randomized patients to a fixed empiric AV delay, echocardiographic optimization of AV delay, or AV delay optimization based on the SmartDelay® algorithm. The SmartDelay algorithm is an electrogram based method derived from invasive hemodynamic studies that measured acute changes in LV dP/dtmax with biventricular pacing. Methods: 1014 patients (68% male, mean age 66±11 years, mean LVEF: 25%±7%) who met enrollment criteria received a CRT-D, and were randomized in 1:1:1 ratio to three arms: AV delay set at 120 msec, AV delay programmed using echocardiography (mitral inflow method) or AV delay programming using the SmartDelay algorithm. Patients were programmed to either DDD or DDDR with a lower rate of 60 and were evaluated at baseline and 3 and 6-months post-implant. Variables measured included: clinical status (NYHA class, quality of life score, 6 minute walk distance, HF hospitalization), plasma biomarker profiles, and 2D echocardiographic-derived volumes Results: The primary endpoint of change in ejection fraction was 6% at 6 months by 3 groups will be presented. Secondary endpoints including NYHA classification, 6 minute walk distance, changes in quality of life and HF hospitalizations will be presented. Initial results regarding changes in biomarker profiles as they relate to the primary endpoint will also be presented. Conclusion: The SMART-AV trial measured the effects of AV optimization by different methods on structural and functional outcomes. The potential implications for non-responders will be discussed.

Author Disclosures: A.F. Hernandez: Research Grant; Significant; Johnson & Johnson, Honoraria; Most; Amgen, Corthera, C.M. O’Connor: Research Grant; Significant; Johnson & Johnson, Honoraria; Most; Other Research Support; Significant; Merck, R.C. Starling: Research Grant; Most; Johnson & Johnson, P.W. Armstrong: Research Grant; Significant; Johnson & Johnson, K. Dickstein: Johnson & Johnson, D. Genovesio: Employment; Significant; Johnson & Johnson, V. Hasselblad: None, G.M. Heizer: None, M. Komajda: Research Grant; Significant; Johnson & Johnson, B. Massie: Johnson & Johnson, J.J. McMurray: Johnson & Johnson, K. Nieminen: Johnson & Johnson, C.J. Reis: None, J.L. Rouleau: Johnson & Johnson, K. Sweedberg: Johnson & Johnson, R.M. Califf: Johnson & Johnson.

Efficacy and Safety of Prescription Omega-3-Acid Ethyl Esters (P-OM3) for the Prevention of Recurrent Symptomatic Atrial Fibrillation (AF)

Peter R Kowey, Main Line Health Heart Cntr Lankenau Hosp, Wynnewood, PA; James A Reiffel, Columbus Med Ctr, New York, NY; Kenneth A Ellenbogen, Virginia Commonwealth Univ Med Ctr, Richmond, VA; Gerard V Naccarelli, Penn State Univ College of Medicine, Hershey, PA; Craig M Pratt; Methodist Debakey Heart & Vascular Ctr, Houston, TX

Objectives: AF is common and usually requires therapy; yet, current treatments have limited efficacy and untoward side effects. Data from several small trials suggest antiarrhythmic benefits of omega-3 polyunsaturated fatty acids may be effective and are safe. We conducted a prospective, randomized, double-blind study to evaluate efficacy and safety of P-OM3 in patients with confirmed symptomatic paroxysmal or persistent AF. Methods: Subjects with symptomatic AF without significant structural heart disease were eligible. Concomitant antiarrhythmic drugs were not allowed. The primary endpoint was time to first recurrence of symptomatic AF. Patients with paroxysmal AF secondary analysis of outcomes included patients with paroxysmal AF. Results: 204 patients with paroxysmal (n=101) and/or persistent (n=103) AF were randomized to P-OM3 4 g/dl or placebo and treated for 24 weeks. The treatment groups and strata were well matched with regard to demographics and/or risk factors. The median age was 66% male, with 67% concomitant beta blocker use, 45% statin use, 39% ACE/ARB use; 62% had hypertension, 17% had CAD, and 3% had clinically significant abnormal baseline ECHO. There was no difference between treatment groups in the time to first recurrence of symptomatic AF in the paroxysmal stratum (HR 1.015, CI 0.9–1.014; p = 0.263). Similar results were observed in the persistent stratum and both groups combined. Secondary analyses support the primary
result. P-OM3 was safe and well tolerated; 5% of placebo and 4% of P-OM3 treated patients discontinued due to AEs. EPA and DHA blood levels were significantly higher in the P-OM3 group compared to placebo (p<0.001) and heart rate was lower. Conclusion: This study demonstrates no benefit of P-OM3 for the prevention of recurrent AF in subjects without significant structural heart disease. Study funded by GlaxoSmithKline, Research Triangle Park, NC

Kaplan-Meier Plot of Time to Event from First Dose of Study Drug to First Recurrence of Symptomatic Atrial Fibrillation/Flutter by Treatment Group in Subjects with Paroxysmal Atrial Fibrillation

Subjects At Risk

P 25% 50% 75% 90% 100%

P258 269 286 297 305 314

HR = hazard ratio. Analysis based on a Cox proportional hazards model adjusting for treatment, region, ACEI/ARB use, and statin use.


CLOSURE I: A Prospective, Multicenter, Randomized Controlled Trial to Evaluate the Safety and Efficacy of the STARFlex® Septal Closure System versus Best Medical Therapy in Patients With a Stroke or Transient Ischemic Attack Due to Presumed Paradoxical Embolism Through a Patent Foramen Ovale

Anthony Furlan, Univ Hosp Case Neurological Institute, Cleveland, OH; Joseph Massaro, Harvard Clinical Resch Institute, Boston, MA; Laura Mauri, HCRI, Boston, MA; Harold Adams, Univ of Iowa, Iowa City, OH; Gregory Albers, Stanford, Palo Alto, CA; Robert Feibig, Geisinger, Danville, PA; Howard Herrmann, Univ of Pennsylvania, Philadelphia, PA; Saibil Kar, Cedars Sinai Med Ctr, Los Angeles, CA; Michael Landzberg, Brigham and Women’s Hosp, Boston, MA; Albert Riazner, Methodist Hosp, Houston, TX; Lawrence Wechsler, Univ of Pittsburgh, Pittsburgh, PA; Mark Reisman; Swedish Med Ctr, Seattle, WA

Background: Some strokes with unknown etiology (cryptogenic) may be the result of paradoxical embolism traversing a patent foramen ovale (PFO). The utility of percutaneous devices for secondary prevention in patients with cryptogenic stroke or transient ischemic attack (TIA) and PFO not associated to medical therapy alone is not known. CLOSURE I is the first completed randomized controlled trial comparing the safety and efficacy of percutaneous PFO closure to medical therapy alone for secondary TIA and stroke prevention in patients with PFO. The main results of CLOSURE I will be presented. Study Objective: The primary objective of CLOSURE I is to determine whether percutaneous PFO closure utilizing the STARFlex® Septal Closure System in combination with medical therapy is superior to medical therapy alone for the prevention of recurrent TIA, stroke, and mortality in patients with cryptogenic TIA or stroke and PFO. Study Design: CLOSURE I is a prospective, multi-center, randomized, open-label, two-arm superiority trial. The study population includes patients with a cryptogenic TIA or stroke and PFO documented by TEE, with or without atrial septal aneurysm, within 6 months of randomization. Between June 23, 2003 and October 24, 2008, 910 patients age 18–60 were randomized at 87 sites in the USA and Canada to either medical therapy (aspirin 325 mg daily or warfarin target INR 2.0–3.0 or a combination of the two) or percutaneous PFO closure utilizing STARFlex® plus medical therapy (clopidogrel 75 mg for 6 months and aspirin 325 mg for two years). Follow up visits were at 1 month (phone), 6 months, 12 months, and 24 months. The primary endpoint is the 2-year rate of stroke or TIA, all cause mortality for the first 30 days, and neurological mortality ≥ 31 days. Conclusions: CLOSURE I will provide the first randomized controlled trial evidence as to whether percutaneous closure using the STARFlex® Septal Closure System is safe and more effective than medical therapy alone in preventing a recurrent stroke or TIA and mortality in patients with PFO.

Author Disclosures: A. Furlan: Consultant/Advisory Board; modest; Consultant NMT Medicina Inc <10,000/year. J. Massaro: I was paid for my work on this project as a statistician through Harvard Clinical Research Institute, who was the data coordinating center for this project and for whom I am employed part time as a st. L. Mauri: Consulting for Cordis. N. Adams: The chief disclosure is that we are investigators in the trial sponsored by NMT. My other disclosures – Merck and Schering-Plough – research support. G. Albers: My only relevant disclosure information is: consultant for NMT and grant support from NMT (local P of CLOSURE trial). R. Feibig: None. H. Herrmann: Research Grant; modest; Research funding from: S. Kar: Ownership Interest; modest; small stock holdings NMT. Consultant/Advisory Board; modest; SAB member of NMT. M. Landzberg: I have performed research trials associated with NMT, and currently serve on the Executive Committee for CLOSURE I. A. Riazner: NMT Medical Inc. L. Wechsler: NMT Medical Inc. M. Reisman: Dr. Reisman provides consulting services for Boston Scientific and Cordis. Receiving honoraria from both, and does research for NMT and Coherex and receives no royalties from either.

Late-Breaking Clinical Trials III

Hall B

Abstracts 21791–21843

NV1FGF Gene Therapy on Amputation-Free Survival in Critical Limb Ischemia - Phase 3 Randomized Double-Blind Placebo-Controlled Trial

William R Hiatt, Univ of Colorado Denver, Denver, CO; Iris I Baumgartner, Univ Hosp, Berne, Switzerland; Sigrid Nikol, Asklepios Klinik St. Georg, Hamburg, Germany; Eric Van Belle, Hosp Cardiologique, CHRU de Lille, France; Vickie R Driver, Boston Univ Sch of Medicine, Boston, MA; Lars Norgren, Univ Hosp, Orebro, Sweden; Jill J Beich, Univ of Dundee, Dundee, United Kingdom

Background: Patients with critical limb ischemia (CLI) and skin lesions, unsuitable for revascularization have a high rate of amputation and mortality. Local gene therapy using non-viral plasmid DNA encoding acidic fibroblast growth factor (ferferminogene pecaaplasmid, also known as NV1FGF) demonstrated positive phase 2 results on both amputation and mortality in CLI. The TAMARIS phase 3 trial tested the hypothesis that intramuscular injection of NV1FGF would confirm the benefit on amputation-free survival in CLI. Methods: This was a large international trial involving 170 sites in 30 countries, enrolling 525 patients (232 treated) with CLI unsuitable for revascularization who had stable ischemic skin lesions. Patients were included who had a lower extremity ischemic ulcer and met hemodynamic criteria of an ankle pressure <70 mmHg and/or a toe pressure <50 mmHg or a transcutaneous oxygen pressure <30mmHg in the treated leg. Patients were randomized double-blind to receive 8 intramuscular injections on the same leg of either 2.5 ml NV1FGF at 0.2 mg/ml or placebo on Days 1, 15, 29, and 43. The primary endpoint was the reduction of major amputation or death, whichever came first, at 1 year analysed with a log rank test using a multivariate Cox proportional hazard model. The sample size was based on an assumed annual event rate of 51.5% on placebo and 33.2% on NV1FGF (90% power, alpha 5%). Results: Patients had a mean age of 70 ± 10 years, 70% were male, 53% had diabetes, 61% had a history of smoking and 54% had a history of coronary artery disease. The results demonstrated no benefit of the treatment on the primary endpoint or components of the primary. During the conduct of the trial there were no major safety concerns.

Standard versus High-Dose Clopidogrel According to Platelet Function Testing After PCI: Results of the GRAVITAS Trial

Matthew J Price; Scripps Clinic, La Jolla, CA

Background: Observational, single-center studies have suggested an association between high residual platelet reactivity on clopidogrel therapy and cardiovascular events after percutaneous coronary intervention. Methods: In this multicenter, blinded, placebo-controlled, randomized trial, we compared high-dose clopidogrel (additional loading dose, 150-mg daily thereafter) with standard-dose clopidogrel (no additional loading dose, 75-mg daily thereafter) for the prevention of cardiovascular events after percutaneous coronary intervention with drug-eluting stents in 2,214 patients with high residual platelet reactivity according to the VerifyNow P2Y12 Test (Accumetrics, San Diego, CA), measured 12 to 24 hours after the procedure. A cohort of 586 patients without high residual platelet reactivity selected at random were also enrolled and treated in a blinded fashion with standard-dose clopidogrel (75-mg daily). The primary efficacy endpoint was a composite of death from cardiovascular causes, myocardial infarction, or stent thrombosis at 6 months follow-up. Results: The primary results of the trial will be presented. Conclusions: GRAVITAS is the first large-scale clinical trial designed to examine whether adjustment of antiplatelet therapy on the basis of platelet function testing using a point-of-care assay improves outcomes after PCI with DES.

Author Disclosures: M.J. Price: Research Grant; modest; Accuretixics. Research Grant; significant; BMS/Sanofi-aventis. Speakers Bureau; significant; DS/I Eli Lilly, Honors; modest; The Medicines Company. Consultant/Advisory Board; modest; BMS/Sanofi-Aventis. Consultant/Advisory Board; significant; DS/I Eli Lilly, Accuretixics.
Late Cardiac Death and Myocardial Infarction Associated With Late Stent Thrombosis in Large Vessel Stenting After 1st or 2nd Generation Drug-Eluting Compared to Bare-Metal Stents: the BASKET PROSpective Evaluation ExamINATION (BASKET PROVE)

Matthias E Pfisterer, Christoph A Kaiser; Univ Hosp, Basel, Switzerland

Background: BASKET long-term outcome data suggested that patients with large native vessel stenting were at increased risk of late stent thrombosis and related cardiac death and myocardial infarction (MI) after 1st generation drug-eluting stent (DES) compared to bare-metal stent (BMS) implantation. We tested the hypothesis whether this could be confirmed in an adequately sized prospective randomized controlled trial and whether this was also true for 2nd generation DES. Methods: Thus, in a multicenter study, 2314 consecutive patients with ≥3.0mm stents were randomized to receive a Cypher-Select or a Vision stent - as in BASKET - or a XienceV stent. The primary endpoint was cardiac death or MI after two years. Late events, months 7–24, and target-vessel revascularization (TVR) were main secondary safety and efficacy endpoints. Results: Patients presented with acute coronary syndrome in 65%, 76% had ≥1 "off-label" indication for drug-eluting stenting. Two-year cardiac death or non-fatal MI rate was 3.6%, not significantly different between the 3 study groups. Results were similar also for cardiac death, MI or stent thrombosis. However, compared to BMS, TVR rate was reduced by both DES by >50% (both p <0.01 versus BMS), with similar 2-year TVR rates for both DES. Conclusions: Late safety problems of DES could not be confirmed in contemporary stenting of large coronary arteries. Between 1st and 2nd generation DES, no safety or efficacy differences could be detected. Both DES reduces TVR more than BMS.


Late-Breaking Clinical Trials IV
Room S100a
Abstracts 21685–21826

The Anglo-Scandinavian Cardiac Outcomes Trial (ASCOT): Testing C-Reactive Protein as Baseline and on-Treatment as an Independent Predictor of Cardiovascular Outcomes

Peter S Sever, Neil R Poulter, Choon-Lan Chang, Simon A Thom, Alan D Hughes, Imperial College London, London, London, United Kingdom; Paul Weilsh, Naved Sattar; Univ of Glasgow, Glasgow, United Kingdom

Background Lowering C-reactive protein (hsCRP) by statins has been shown to independently predict cardiovascular (CV) outcomes. In a nested case-control study we explore the relationship between biomarkers prior to, and in-trial, with blood pressure and lipid lowering therapy, and CV outcomes. Methods: In UK and Ireland, ASCOT randomised 9088 hypertensive adults to either calcium channel blocker- or beta blocker-based treatment. 4853 patients with total cholesterol <6.5 mmol/L (250mg/L) were further randomised to atorvastatin or placebo. Over 5.5 years, 485 CV cases (fatal coronary heart disease, non-fatal MI, coronary revascularisation, fatal or non-fatal stroke) were age and sex matched with 1367 controls. Conditional logistic regression models were used to evaluate the association between CV events and LDL-cholesterol (LDL-c) and hsCRP. Results: Baseline LDL-c and hsCRP were significantly correlated (r=0.11, p<0.0001) and predicted CV events (odds ratio [OR] 1.31 [CI 1.10–1.56, p=0.002], and OR 1.19 [CI 1.05–1.34, p=0.008] respectively). Both ORs per 1–SD increase in log-transformed data. However, inclusion of hsCRP into the Framingham risk model only minimally improved prediction of CV events. At 6 months, atorvastatin reduced LDL-c by 40.3% and median hsCRP by 27.4%. In those randomised to atorvastatin, lower in-tial LDL-c < median (2.1mmol/L) at 6 months was associated with a highly significant reduction in CV events (OR 0.41 [CI 0.22–0.75, p=0.004]) compared with those with median LDL-c, in a fully adjusted model incorporating other baseline risk factors. By contrast, in those randomised to atorvastatin, in the fully adjusted model, lower hs CRP at 6 months was not associated with CV events (OR 0.86 [0.49–1.51, p=0.60]) compared with those with median hsCRP levels. Consequently, addition of on-treatment hsCRP to on-treatment LDL-c did not improve prediction of CV outcomes. Conclusion: These analyses do not support the hypothesis that hsCRP usefully improves risk factor prediction or indeed that a reduction in hsCRP associated with statin therapy is an independent predictor of CV outcomes.

Author Disclosures: P.S. Sever: Research Grant; Significant; Pfizer. Speakers Bureau; Significant; Pfizer. S.A. Thom: Research Grant; Significant; Pfizer. N.R. Poulter: Research Grant; Significant; Pfizer. Speakers Bureau; Significant; Pfizer. N. Sattar: Research Grant; Significant; Pfizer. Add. A.D. Hughes: Pfizer. P. Welsch: Pfizer. N. Sattar: Pfizer.

Primary Results of the DEFINE trial: Determining the Efficacy and Tolerability of CETP Inhibition With AnacEtrapid

Christopher P Cannon, TIMI Study Group, Bostom, MA; Sucret Shah, Hayes M Dansky, Merck, Rahway, NJ; Michael Davidson, Univ of Chicago Med Cente, Chicago, IL; Erol A Dogru, Univ of Utah Sch of Medicine, Salt Lake City, UT; Antonio M Gotto, Jr., Cornell Med Sch, New York, NY; Michael Stepanavage, Sherry Xueyu Liu, Patrice Gibbons, Tanya B Ashraf, Jennifer Zafarino, Yale B Mitchell, Merck, Rahway, NJ; Philip Barter; Heart Rock Institute, Sydney, Australia

Background: New therapies to raise HDL-C are currently being investigated as a strategy to reduce residual cardiovascular risk. Anacetrapib is a cholesteryl ester transfer protein (CETP) inhibitor with robust HDL-C raising and LDL-C lowering effects and no adverse effects on blood pressure, electrolytes and aldosterone levels. Methods: Determining the Efficacy and
Tolerability of CETP Inhibition with Anacetrapib (DEFINE) is a randomized, double-blind, placebo-controlled trial to assess the efficacy and safety profile of anacetrapib in patients with coronary heart disease (CHD) or CHD risk-equivalents (clinical trials.gov NCT00685776). Eligible patients, who are treated to NCEP-ATP III LDL-C treatment goal with a statin ± other lipid-modifying medications, are randomized to anacetrapib 100 mg or placebo for 18 months, followed by a 3 month post-study follow-up. The primary endpoints are percent change in LDL-C and the safety and tolerability of anacetrapib, including the evaluation of adjudicated major adverse CV events. Results: A total of 2757 patients were screened at 153 centers in 20 countries and 1623 patients were randomized into the trial. Lipid results, clinical CV events and other safety assessments for the 18-month treatment phase will be completed in September 2010 and will be available for presentation at the AHA meeting in November 2010. 

Tolerability of CETP Inhibition with Anacetrapib (DEFINE): Results from the 18-Month Treatment Phase

Symplicity HTN-2: International, Multicenter, Prospective, Randomized, Controlled Trial of Endovascular Selective Renal Sympathectomy for the Treatment of Hypertension

Murray Ester; Baker IDI Heart and Diabetes Institute, Melbourne, Victoria, Australia

Background: Renal sympathetic afferent and efferent nerves play a seminal role in mediating hypertension. The objective of this international, multicenter, prospective, randomized, controlled trial was to demonstrate that endovascular ablation of the renal nerves is a safe and effective treatment for uncontrolled hypertension. Methods: Adults 18–85, with systolic blood pressure >160 mmHg (≥150 mmHg systolic in type II diabetes) despite demonstrated compliance with at least three antihypertensive medications from different drug classes were recruited at 24 centers with ethics committee approval in Europe and Australia. Patients were excretory urogram demonstrated in May 2010 and if renal artery anatomy revealed either significant renal artery stenosis or precluded safe denervation. Subjects were required to demonstrate compliance to medical therapy, before randomization to either therapeutic renal denervation (RDN) with continuing medical therapy or continuing medical therapy (CON); twenty-seven patients were excluded after screening and before randomization when office blood pressure was found to be <160 mmHg after the compliance screening period. The primary endpoint was change in office systolic BP between baseline and 6-months. Secondary endpoints include both acute and chronic procedural safety. Initial Demographics: Between June 2009 and March 2010, 106 patients were randomized: CON 54 and RDN 52. Patients were taking an average 5.3 anti-HTN medications with an average baseline BP of 178/97 to 17/16 mmHg. Patients generally had similar baseline characteristics, with RDN having lower baseline eGFR (77 vs. 87 ml/min) (Table 1). Conclusions: Bilateral renal denervation was successfully performed in 53/52 (100%). There were no serious device or procedure-related complications. Complete effectiveness and safety data will be presented.

Table 1: Baseline Characteristics

<table>
<thead>
<tr>
<th>CON (n=54)</th>
<th>RDN (n=52)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>58 ± 13</td>
<td>59 ± 11</td>
</tr>
<tr>
<td>Gender (% female)</td>
<td>65%</td>
<td>55%</td>
</tr>
<tr>
<td>Type 2 diabetes</td>
<td>28%</td>
<td>31%</td>
</tr>
<tr>
<td>eGFR (mL/min/1.73m²)</td>
<td>78 ± 20</td>
<td>79 ± 19</td>
</tr>
<tr>
<td>Heart Rate (bpm)</td>
<td>78 ± 15</td>
<td>75 ± 15</td>
</tr>
<tr>
<td>Office SBP (mmHg)</td>
<td>179 ± 16</td>
<td>176 ± 12</td>
</tr>
<tr>
<td>Office DBP (mmHg)</td>
<td>98 ± 16</td>
<td>97 ± 16</td>
</tr>
</tbody>
</table>

Clinical Science: Special Reports 1

Room S100c

Abstracts 21838-21821

The Relationship Between Atrial High-Rate Episodes and Stroke: The Asymptomatic Stroke and Atrial Fibrillation Evaluation in Pacemaker Patients (ASERTT) Trial

Jeff S Healey, Stuart J Connolly, McMaster Univ, Hamilton, Canada; Michael R Gold, Med Univ of South Carolina, Charleston, SC; Alessandro Capucci, McMaster Univ Università Politecnica delle Marche, Ancona, Italy; Carsten Israel, Klinik für Innere Medizin – Kardiologie & Angiologie, Bielefeld, Germany; Isabelle C van Gelder, Univ of Groningen, Groningen, Netherlands; Chu-Pak Lau, Queen Mary Hosp, Hong Kong, Hong Kong; Carlos A Morillo, McMaster Univ, Hamilton, Canada; Eric Fain, St Jude Med, Sylmar, CA; Mark Carlson, St Jude Med, Sylmar, CA; Stefan H Höhnleiser, J. W. Goethe Univ, Frankfurt, Germany

Atrial fibrillation (AF) is one of the most important causes of stroke; however, the majority of AF is clinically silent. Modern pacemakers have the ability to document even transient AF. Further time-dependent analyses were conducted for the primary analysis; episodes lasting more than 6 minutes, with a rate >180/minute were considered "clinical" AF. Other analyses were conducted for the primary analysis; episodes lasting more than 6 minutes, with a rate >180/minute were considered "clinical" AF. Other analyses were conducted for the primary analysis; episodes lasting more than 6 minutes, with a rate >180/minute were considered "clinical" AF. Other analyses were conducted for the primary analysis; episodes lasting more than 6 minutes, with a rate >180/minute were considered "clinical" AF. Other analyses were conducted. These brief、“atrial high-rate episodes (AHRE)" are quite frequent in clinical practice. The clarification of their temporal association with stroke will not only determine the need for oral anticoagulation, but will help clarify the precise relationship between AF and stroke. Methods: The ASERTT trial enrolled patients over the age of 65, with a history of hypertension who were receiving a dual-chamber pacemaker for standard indications. The trial included patients with a history of AF and those receiving oral anticoagulation. Following a 4 week lead maturation period, AHRE episodes were collected and were adjudicated by a blinded, central committee. For the primary analysis; episodes lasting more than 6 minutes, with a rate >180/minute were considered significant and patients were categorized as to the presence or absence of such episodes during the first 3 months. The primary outcome was ischemic stroke or non-central nervous system (CNS) systemic embolism. Further time-dependent analyses were conducted.
to explore the relationship between all AHRE and embolic events. **Results:** A total of 2582 patients were enrolled in 23 countries, between December 2004 and September 2008. Follow-up completed in June 2010, after a mean study duration of 43 months. The mean age of patients was 76.7 ± 7 years and 42% were female. All patients had hypertension, 26% had diabetes mellitus, 15% had heart failure and 7% had prior stroke. The mean CHA2DS2-VASc score was 2.41. Only 75% of patients were started on oral anticoagulation during the study. Implanted devices detected AHRE in 60% of patients; adjudication confirmed that only 51% of these episodes were true atrial arrhythmias. The overall rate of the primary outcome composite of non-CNS systemic embolism and ischemic stroke started on oral anticoagulation during the study. Implanted devices detected AHRE in 60% of patients; adjudication confirmed that only 51% of these episodes were true atrial arrhythmias. The overall rate of the primary outcome composite of non-CNS systemic embolism and ischemic stroke was 0.72% per year. This risk correlated strongly with baseline stroke risk factors and was 1.06% per year in patients with a CHA2DS2 score or >1 and only 0.19% per year for those with a CHA2DS2 score = 1. The study has at least 80% power to detect a doubling of embolic risk with the presence of AHRE. Final results will be presented at the meeting.

**Author Disclosures:** J.S. Healey: Research Grant; Significant; T. Stude Medical; S.J. Connolly: None. C. Lau: None. A. Capucci: None. C. Israel: None. I.G. van Gelder: None. C. Lau: None. C.A. Morrill: None. E. Faire: Employment; Significant; St Jude Medical. M. Carlson: St Jude Medical. S.H. Hohklesson: None.

**Impact of Massachussets Health Care Reform on Racial, Ethnic, and Socioeconomic Disparities in Cardiovascular Care**


**Background:** Because insurance status is positively associated with receipt of invasive cardiovascular procedures, we examined the impact of the Massachusetts (MA) Health Care Reform Act on coronary revascularization by race/ethnicity/education level and-in hospital mortality. **Methods:** Using a state database, we compared race/ethnic and educational differences in coronary revascularization [surgery (CABG), percutaneous intervention: stent (PCI)] and in-hospital mortality among all MA residents 21–64 years old with a hospital discharge diagnosis of ischemic heart disease pre (November 1, 2004 to July 31, 2008) and post (December 1, 2008 to September 30, 2008) health reform. **Results:** Crude logistic regression models controlled for age, sex, admission status and comorbidities and multivariable models** additionally adjusted for education; Race/ethnic differences were noted for CABG-PCI procedures pre-reform with no significant change in these disparities post-reform. Increasing education (+high school (HS), HS graduate, >HS) was linked to increased coronary revascularization pre and post-reform (p < 0.001). Post-reform the odds of in-hospital mortality were lower for blacks and higher in Asians than whites. **Conclusion:** MA health reform has thus far not resulted in significant changes in observed race/ethnic/educational disparities in coronary revascularization. Blacks had lower odds of in-hospital mortality post-reform compared to whites.

**Author Disclosures:** M.A. Albert; None. T.S. Silbaugh; None. J.Z. Ayanian; None. A. Lovett; None. R.E. Wolf; None. K. Zelevinsky; None. F. Resnick; None. S. Norman; None.

**Comparative Effectiveness of Exercise Electrocardiography versus Exercise Electromagnetic Tomography Plus Myocardial Perfusion SPECT in Women With Suspected Coronary Artery Disease: Results From the What's the Optimal Method for Ischemia Evaluation in Women Trial**

Leslie J Shaw, Emory Univ Sch of Med, Atlanta, GA; Jennifer H Mieres, Northwestern Univ, Chicago, IL; Dorothy Sullivan, Kimberly Parks, Thomas Wang, Shawn A Gregory, Shammargam Uthamalingam, Marc J Semigran; Massachusetts General Hospital, Boston, MA

**Introduction:** Lower values of amino-terminal pro-B type natriuretic peptide (NT-proBNP) predict favorable prognosis in patients with chronic heart failure (HF). Many HF therapies lower NT-proBNP values, but it is unclear whether titrating HF treatment with the goal of reducing NT-proBNP concentrations is superior to HF care based on standard clinical parameters. In the Prognostically-Oriented Tailored Chronic HF Therapy (PROTECT) Study (NCT00351390), we hypothesized NT-proBNP guided HF care would lead to better outcomes. **Methods:** In a prospective single-center trial, 151 subjects with HF due to left ventricular (LV) systolic dysfunction (ejection fraction ≤ 40%) were randomized to receive either standard HF care or standard HF care plus a goal to reduce NT-proBNP concentrations ≤ 1000 pg/mL. The primary endpoint was total cardiovascular events over a one-year period; secondary endpoints included effects of NT-proBNP guided care on patient quality of life (QOL; assessed with the Minnesota Living with HF Questionnaire) as well as cardiac structure and function, assessed via 2-dimensional echocardiography. **Results:** The mean age was 63 years, 87% were NYHA class II/III; the mean baseline LVEF was 27.9 ± 9.9%. Through 10 months, subjects in the NT-proBNP arm had more office visits for HF care (P = 0.05 versus the standard of care [SOC] arm), and at study completion were less likely than SOC patients to be taking loop diuretics (93% vs 86%, P = 0.05) and more likely than SOC patients to be taking aldosterone antagonists (38% vs 45%, P = 0.001). Those in the NT-proBNP arm had significant lowering of their NT-proBNP value (2344 vs 1125 pg/mL, P = 0.01), with 44% ≤ 1000 pg/mL. SOC arm patients did not have a significant change in their NT-proBNP value (1946 vs 1844 pg/mL, P = 0.61). Compared to SOC, a significant reduction in the primary endpoint of total cardiovascular events was seen in the NT-proBNP arm (100 vs 88; P = 0.09; OR = 0.44, 95% CI: 0.22–0.84; P < 0.02), with particular effects on worsening HF and HF hospitalization (both P < 0.003). Fewer patients in the NT-proBNP group had HF exacerbations (9% vs 29.3%, P = 0.04), Greater improvements in exercise capacity were seen in NT-proBNP patients. **Conclusions:** Among patients with chronic systolic HF, NT-proBNP guided HF therapy was superior to standard HF care.


**Clinical Science: Special Reports II**

Room S100c

**21854 Intraocular Pressure Versus Intraocular Abnormality in ST-Elevation Myocardial Infarction: Results of the CICERO Trial in Patients Undergoing Primary Percutaneous Coronary Intervention With Thrombus Aspiration**

Yosinui L G, Marthe A Kampinga, Wouter G Wierenga, Marije L Fokkema, Ad van den Heuvel, Eng-Shiong Tan, Gabija Puntikite, Rik van der Werf, Syroos Hoseyni Guyom, Felix Zijlstra, Bart J de Smet, Univ Med Cntr Groningen, Univ of Groningen, Groningen, Netherlands

**Background Administration of the glycoprotein IIb/IIIa inhibitor abciximab is an effective adjunctive treatment strategy during primary percutaneous coronary intervention (PCI) for ST-elevation
myocardial infarction (STEMI). Although small-scaled studies have suggested beneficial effects of intracoronary (IC) over intravenous (IV) administration, it is uncertain whether this route is more effective. This trial investigated whether IC administration of abciximab is superior to IV administration in improving myocardial reperfusion in patients undergoing primary PCI with thrombus aspiration. Methods: The CEDERO trial, a single-center prospective randomized open-label trial with blinded evaluation of endpoints, randomized STEMI patients undergoing primary PCI with thrombus aspiration within 12 hours of symptom onset to either an IC or IV bolus of abciximab (0.25 mg/kg). Patients were pre-treated with aspirin, heparin, and clopidogrel. The primary endpoint was the incidence of restored myocardial reperfusion, defined as complete ST-segment resolution (STR). Secondary endpoints included myocardial reperfusion as assessed by myocardial blush grade (MBG), enzymatic infarct size defined by peak creatinine kinase (CK), myocardial band fraction of CK (CK-MB), and cardiac troponin T (cTNT), and major adverse cardiac events (MACE) at 30 days. Results: A total of 534 patients (64%≤13 years, 74% male, 12% diabetics, and 4% anterior infarction) were randomized between September 2009 and April 2010. The incidence of complete STR was similar in the IC and IV groups (64% vs 62%, p=0.562). However, the incidence of MBG 2/3 was higher in the IC group than in the IV group (76% vs 67%, p=0.022). Furthermore, enzymatic infarct size was approximately 30% smaller in the IC than in the IV group (p=0.008). The incidence of MACE was similar in both groups (5.5% versus 6.1%, p=0.78%). Conclusion: In patients undergoing primary PCI with thrombus aspiration, IC administration of abciximab is not superior to IV in improving myocardial reperfusion as assessed by STR. However, IC administration is associated with improved myocardial reperfusion as assessed by MBG and a smaller enzymatic infarct size.


A Randomized Placebo Controlled Trial of Intravenous Erythropoietin to Reduce Infarct Size After ST-Segment Elevation Myocardial Infarction: Primary Results of the REVEAL Trial


Background: Acute myocardial infarction is a leading cause of morbidity and mortality. Preclinical studies have demonstrated that Erythropoietin exerts an important cytoprotective effect in experimental models of myocardial injury. We evaluated the safety and efficacy of a single infusion of erythropoetin alfa in patients with STEMI-elevation myocardial infarctions (STEMI). Methods and Results: 136 Patients with STEMI who underwent successful percutaneous coronary intervention (PCI) within 8 hours of symptom onset were randomized to 60,000 units of intravenous erythropoetin alfa or matching saline placebo administered within 4 hours of reperfusion. The primary endpoint was infarct size assessed by cardiac magnetic resonance imaging study 2–6 days after study medication administration. Secondary endpoints included infarct size by CMR at 3 months as well as death, recurrent MI, unplanned PCI, and major adverse cardiac events (MACE) at 30 days. Enzymatic infarct size was approximately 30% smaller in the IC than in the placebo group (19.9±9.9% 11.7±7.2%, p=0.022). Furthermore, the early (15.8±0.7% vs. 10.3% vs. 10.0%, p=0.78%). Conclusion: In patients undergoing primary PCI with thrombus aspiration, IC administration of abciximab is not superior to IV in improving myocardial reperfusion as assessed by STR. However, IC administration is associated with improved myocardial reperfusion as assessed by MBG and a smaller enzymatic infarct size.


Time-Based SStategy to Reduce Clopidogrel AssociaTed Bleeding DuRing CABG. Results From the TARGET CABG Study

Elisabeth Mahla, Mark Antonino, Thomas Suarez, Kevin P Bleden, Alex Sequeria, Peter Chow, Udaya Tantry, Paul A Gurbel; Sinai Hosp Baltimore, Baltimore, MD

Background: Guidelines recommend withholding clopidogrel for 5 hours to aspirin treatment evaluated with the PFA100 method and platelet aggregometry with AA did not reduce infarct size, and may increase infarct size and major adverse cardiac events in older patients.


Chest tube drainage and blood product usage were determined over 24 hours. Cardiac marker release and ischemic event data will be analyzed. Results: There was no greater bleeding in the TEG-guided patients who underwent CABG earlier (2.5 +/- 1.7 days) than the recommended ACC/AHA guidelines. Red blood cells transfusion and chest tube drainage were not greater in the TEG-guided group of patients as compared to non-guided patients. In addition, CABG was induced an immediate reduction in platelet counts and function (Table). Despite persistent low platelet count, platelet function rose to preoperative levels at 24 hrs post-CABG. Conclusions: This is the first prospective study to demonstrate that the timing of CABG can be optimized by an objective measurement of platelet function by TEG in clopidogrel treated patients. Patients on clopidogrel therapy can safely undergo earlier CABG than recommended by guidelines when the timing of the surgery is guided by TEG based platelet function measurement.

The Results of the ASCET Trial

Atle-Aage Petterssen, Ingeborg Seljeflot, Dept of Cardiology, Oslo Univ Hosp, Ulleval, Oslo, Norway; Michael H Abdelnoor, Ctr for Clinical Risch, Oslo Univ Hosp, Ulleval, Oslo, Norway; Harald Arnesen; Dept of Cardiology, Oslo Univ Hosp, Ulleval, Oslo, Norway

Background: Patients with coronary artery disease (CAD) on single antiplatelet therapy still have a high risk for athereothrombotic events. Aspirin non-responsiveness has been discussed as a risk factor for thromboembolic events. There is a need for validated tools that can identify patients with a high on-treatment residual platelet reactivity (RPR) as a guide to change or intensify antiplatelet treatment. Aims and methods: The ASCET study is the first prospective, randomized trial aimed to investigate the relation of platelet function tests to clinical outcome in patients with symptomatic, stable CAD on single antiplatelet therapy. Patients (n=1001) with stable CAD, all verified with coronary angiography and on aspirin 160 mg/d, were randomized to continue treatment with aspirin 160 mg/d or clopidogrel 75 mg/d. Platelet function was assessed at randomization with the PFA100 method and platelet aggregation. Compliance was assessed by determination of serum thromboxane B2. The patients were followed up for two years. The primary end-point was a composite of all-cause death, non-fatal myocardial infarction, ischemic stroke and unstable angina. Major and minor bleedings were registered.

Results: The total number of primary endpoint was 106. No difference in event rates between the randomized groups was observed (56/503 on aspirin, 50/498 on clopidogrel, p=0.57). The prevalence of RPR with the PFA100 method (aspirin non-responders) was 26% at randomization, when compliance to aspirin medication was excellent. After randomization, high on-treatment RPR in the aspirin group evaluated with PFA100 did not influence on the primary endpoint (13.1% vs 13.5%, p=0.41). Platelet aggregation measures with arachidonic acid (AA) did also not predict clinical outcome. Aspirin non-responders randomized to clopidogrel had a non-significant reduction in the combined endpoint compared to aspirin non-responders randomized to continued aspirin treatment (7.8% vs 13.1%, p=0.16). Conclusion: Response to aspirin treatment evaluated with the PFA100 method and platelet aggregation with AA did
Health-Related Quality of Life After Transcatheter Aortic Valve Implantation vs. Non-Surgical Therapy Among Inoperable Patients With Severe Aortic Stenosis: Results From the Randomized PARTNER Trial (Cohort B)

David J Cohen, Saint Luke’s Mid America Heart Institute, Kansas City, MO; Matthew R Reynolds, Harvard Cardiovascular Research Institute, Boston, MA; Yang Lei, Elizabeth M Mahoney, Saint Luke’s Mid America Heart Institute, Kansas City, MO; Lars G Svensson, E M Tuzcu, Cleveland Clinic, Cleveland, OH; Jeffrey W Moses, Columbia Univ Med Ctr, New York, NY; John G Webb, St. Paul’s Hosp, Vancouver, Canada; Michael Mack, Baylor Health System, Dallas, TX; D C Miller, Stanford Univ Med Ctr, Palo Alto, CA; Augusto Pichard, Washington Hosp Ctr, Washington, DC; Raj Makkar, Cedars Sinai Med Ctr, Los Angeles, CA; Howard C Herrmann, Hosp of the Univ of Pennsylvania, Philadelphia, PA; Peter Block, Emory Univ Hosp, Atlanta, GA; Craig R Smith, Martin B Leon; Columbia Univ Med Ctr, New York, NY

Background: Recently, transcatheter aortic valve implantation (TAVI) has been developed as a less-invasive alternative to aortic valve replacement (AVR) for patients with severe aortic stenosis (AS). However, the impact of TAVI on patients’ functional status and health-related quality of life (HRQOL)—particularly in comparison to non-surgical therapies—is unknown. We therefore performed a prospective HRQOL study in conjunction with the Placement of Aortic Transcatheter Valves (PARTNER) Trial. Methods: Between 5/07 and 3/09, 358 patients with severe, symptomatic AS who were determined to be “inoperable” for surgical AVR by a multidisciplinary committee were randomized to either TAVI using the Edwards-SAPIEN valve (n=179) or control standard therapies (including balloon aortic valvuloplasty as required) (n=179). HRQOL was assessed for all patients at baseline, 1, 6, and 12 months after randomization using validated instruments including the Kansas City Cardiomyopathy Questionnaire (KCCQ), SF-12 Health Status Survey, and the EuroQOL (EQ-5D). Results: Baseline characteristics were well-matched between the 2 treatment groups. The mean age was 83 years, 54% were female, 37% had undergone previous CABG, 23% had severe COPD, 15% had porcelain aortas, and 13% had either chest wall radiation or severe deforms. Predicted 30-day mortality was 11.7% according to the STS risk score. Baseline HRQOL demonstrated substantial impairment for both generic and disease-specific measures (see Table). Follow-up HRQOL comparisons were made between groups and between the TAVI and standard therapy groups will be presented. Conclusions: HRQOL is markedly reduced among patients with severe AS who are not candidates for surgical AVR. Direct comparison of the HRQOL benefits of TAVI vs. standard non-surgical therapies should provide important insight into both the magnitude and duration of benefit among this highly complex patient population.

Table 1. Baseline QOL Results

<table>
<thead>
<tr>
<th>QOL Scale</th>
<th>TAVI (n=179)</th>
<th>Control (n=179)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SF-12 Physical*</td>
<td>28.2 ± 7.7</td>
<td>27.7 ± 6.9</td>
</tr>
<tr>
<td>SF-12 Mental Component*</td>
<td>44.5 ± 12.2</td>
<td>45.2 ± 11.0</td>
</tr>
<tr>
<td>KCCQ Subscales**</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Physical Limitations</td>
<td>34.6 ± 25.7</td>
<td>30.7 ± 24.9</td>
</tr>
<tr>
<td>Symptoms</td>
<td>47.7 ± 22.6</td>
<td>46.0 ± 24.0</td>
</tr>
<tr>
<td>Social Limitation</td>
<td>27.8 ± 26.9</td>
<td>26.6 ± 25.9</td>
</tr>
<tr>
<td>Quality of Life</td>
<td>33.6 ± 21.7</td>
<td>32.8 ± 22.9</td>
</tr>
<tr>
<td>Functional Status</td>
<td>41.7 ± 21.9</td>
<td>38.6 ± 21.2</td>
</tr>
<tr>
<td>KCCQ Summary</td>
<td>36.1 ± 20.5</td>
<td>34.4 ± 20.1</td>
</tr>
<tr>
<td>EQ-5D Utilities</td>
<td>0.59 ± 0.23</td>
<td>0.57 ± 0.23</td>
</tr>
</tbody>
</table>

* SF-12 scores have a population mean ± standard deviation of 50 ± 10
** KCCQ scores range from 0-100 (higher scores indicate better QOL)


Clinical Science: Special Reports III

Room S100c

Abstracts 21829–21835

Telemonitoring to Improve Outcomes after Heart Failure Hospitalization: A Randomized Clinical Trial

Sarwat I Chaudhry, Yale Univ Sch Medicine, New Haven, CT; Jennifer A Mattera, Yale-New Haven Hosp, New Haven, CT; Jeptha P Curtis, Beth Hodshon, Jep Herrin, Yale Univ Sch Medicine, New Haven, CT; Zhengqi Lin, Yale-New Haven Hosp, New Haven, CT; John A Sportus, Mid America Heart Institute of St. Luke’s Hosp, St. Louis, MO; Christopher O Phillips, Morehouse Sch of Medicine, Atlanta, GA; Harlan M Krumholz; Yale Univ Sch Medicine, New Haven, CT

Introduction: Telemonitoring, the use of communication technology to monitor clinical status, may improve the care of patients with heart failure symptoms and weight. Direct comparison of the HRQOL benefits of TAVI vs. standard non-surgical therapies should provide the opportunity for intervention before patients become severely ill and require hospitalization. Patients’ participation in the program could favorably affect their health behaviors. Hypothesis: Daily telemonitoring of heart failure symptoms and self-reported body weight will reduce the combined outcome of all-cause readmission or death by at least 25% within 6 months of hospital discharge. Methods: 1653 patients hospitalized for heart failure across the U.S. were enrolled in the trial within 30 days of discharge. Patients randomized to the intervention group were instructed to make a daily, toll-free call to an interactive voice response system (Pharos Innovations, Northfield, IL). On each call, patients were asked to respond to pre-recorded questions about heart failure symptoms and body weight using the telephone keypad. The information was transferred to a secure Internet site for review by clinicians. Patients assigned to usual care received heart failure educational materials and a web-based care plan. The intervention was implemented, and all outcomes were assessed during the 180 days following study enrollment. The study was designed to have 90% power to detect a 25% relative risk reduction in the primary endpoint of either all-cause rehospitalization or death within 180 days. The study is funded by the National Heart, Lung, and Blood Institute. Results: Enrollment is complete and assessment of all outcomes will be finalized by July 31, 2010. The study results will be finalized for presentation at the AHA Scientific Sessions. Conclusions: We will present the results of the largest randomized controlled telemonitoring study of an interactive voice response system for patients recently hospitalized with heart failure. With growing interest in reducing readmissions for heart failure, data on the effectiveness of a simple, non-invasive, hardware-free remote monitoring system can inform practice and policy decisions regarding the use and reimbursement for this strategy.


State-Wide Care is Improved in the Reperfusion of Acute MI in Carolina Emergency Department Emergency Response (RACE-ER) Systems Improvement Program

Christopher B Granger MD, Duke Clinical Rsch Inst, Durham, NC; Lisa M Monk RN, MSJ, Novant Health, Winston-Salem, NC; Mayme I Roettig RN, MSN, HSUS, Hussein Al-Khalidi PhD, Duke Clinical Rsch Inst, Durham, NC; Robert J Applegate MD, Wake Forst Univ, Winston-Salem, NC; Claire C Corbett MMS, NWEMS-P, New Hanover Regional Med Ctr, Wilmington, NC; J L Garvey MD, Carolina’s Med Ctr, Charlotte, NC; William R Hathaway MD, Mission Memorial Hosp, Asheville, NC; B H Wilson MD, Carolina’s Med Ctr, Charlotte, NC; James G Jolls MD; Duke Clinical Rsch Inst, Durham, NC

Background/objective: ACC/AHA Guidelines now recommend development of systems of STEMI care, including a focus on reducing first medical contact to reperfusion. Our objective was to extend the prior NACE project to integrate care in all hospitals and EMS systems in North Carolina to increase speed and rate of reperfusion. Methods: We measured delays of coronary reperfusion using ACTION Registry/Get With The Guidelines in STEMI patients from July 2008 through December 2009, including before (July to September 2008) and 3 months after (September to December 2009) a year-long implementation in the 21 percutaneous coronary interventions (PCI) hospitals and 98 without PCI (non-PCI hospitals, of which 52 routinely transferred patients for primary PCI), and over 500 associated EMS systems. The intervention focused on early diagnosis, early reperfusion activation, and optimizing performance at each point of care: EMS, emergency department, catheterization laboratory, and transfer. Results: Preliminary results show that 6822 STEMI patients treated at PCI hospitals over the course of the study (1068 presented directly to PCI centers and 1179 was transferred) presented directly to PCI centers and 43% were transferred from non-PCI centers. Of direct presenters, patients presented via EMS 69% of the time and 76% post-intervention. Median reperfusion times significantly improved according to first door-to-device (p=0.0001; presenting to PCI hospital 67 to 46 minutes; transferred to PCI hospital among transfer-designated centers 118 to 108 minutes, p=0.01), and first medical contact to device (p<0.0001; presenting to PCI hospital via EMS 103 to 91 minutes). While both significantly improved, the post-intervention proportion of patients with transfer first door to device was only 32% < 90 minutes and 64% < 120 minutes. Eligible but not treated with reperfusion dropped from 5.5% to 4.0%. In contrast to RACE data from 2006 when in-hospital mortality was 7.5%, mortality was 5.8% pre and 5.6% post intervention. Conclusions: A comprehensive state-wide program focused on regional systems for reperfusion for STEMI can significantly improve quality of care, and ongoing improvements as guided by Mission: Lifeline are needed.

Author Disclosures: C.B. Granger MD: Research Grant; Significant: Sanofi-Aventis, Genentech, Boehringer Ingelheim, BMS. Consultant/Advisory Board; Moderate; Novartis, Roche., Consultant/
Comparative Effectiveness of Two Telephone-Delivered Behavioral Interventions to Improve Hypertension Control. Primary Outcomes of a Randomized Controlled Trial

Sundar Natarajan, Jennifer Friedberg, Michelle Ulmer, Iris Lin, Donald Robinaugh, VA New York Harbor Healthcare System, New York, NY; John Allegrante, Teachers College, Columbia Univ, New York, NY; Judith Wylie-Rosett, Albert Einstein College of Medicine, Bronx, NY; Stuart R Lipitz, Brigham and Womens Hosp, Boston, MA

Introduction: The effectiveness of blood pressure (BP) control (systolic BP [SBP] < 130 mm Hg and diastolic BP [DBP] < 80 mm Hg in diabetes or kidney disease, or SBP < 140 mm Hg and DBP < 90 mm Hg in all others) in preventing cardiovascular events is proven. Despite this, a large gap exists between ideal control rates and what is achieved in clinical practice. Although several behavioral trials to improve BP have been reported, the BP control achieved was modest. Few, however, used novel telehealth approaches to target patients with uncontrolled BP in primary care settings. Methods: Using a 3-arm, randomized controlled trial, we evaluated the effect of a stage-matched intervention (SMI) or a health education intervention (HEI) to improve BP control in adults with uncontrolled BP despite treatment with antihypertensive drugs for ≥6 months; usual care (UC) served as control. The SMI and HEI groups received monthly phone counseling targeting diet, exercise and BP medication adherence for 6 months; the SMI used the Transtheoretical Model to tailor counseling while HEI received nontailored education using national guidelines. All participants made study visits at baseline, 3, and 6 months. BP, the primary outcome, was assessed from the mean of 6 readings and categorized as controlled or not. Comparisons between groups were by 2 tests. Results: We recruited and randomized 533 participants with sustained uncontrolled BP from 2 large hospital-based outpatient clinics. There were no differences between groups at baseline. The baseline BP control rates were 42.6%, 40.6%, and 44.8% in SMI, HEI, and UC (p = .74). The 6 month BP control rates were 62.3% (SMI), 52.4% (HEI), and 47.2% (UC) with p values for pairwise comparisons being .016 (SMI vs. UC), .280 (HEI vs. UC), and .066 (SMI vs. HEI). Further, the change in BP control from baseline to 6 months by arm were 19.5% (SMI), 11.9% (HEI) and 6.2% (UC) with p values for the null hypothesis of change = 0 within each arm being 0.00003 (SMI), 0.012 (HEI) and 0.007 (UC). Conclusions: SMI improved BP control compared to both UC and HEI. Both SMI and HEI improved BP control compared to their own baseline. SMI constitutes a new, more potent and potentially cost-effective approach to assisting patients with sustained uncontrolled hypertension reach BP control goals.

Author Disclosures: S. Natarajan: None; J. Friedberg: None; M. Ulmer: None; I. Lin: None; D. Robinaugh: None; J. Allegrante: None; J. Wylie-Rosett: None; S.R. Lipitz: None.

Telemedical Interventional Monitoring in Heart Failure (TIM-HF), a Randomized, Controlled Intervention Trial Investigating the Impact of Telemedicine on Mortality in Ambulatory Patients With Chronic Heart Failure

Friedrich Köhler, Sebastian Winkler, Charité CCM, Dept of Cardiology, Berlin, Germany; Michael Schieber, Udo Sechtem, Robert-Bosch-Krankenhaus Stuttgart, Dept of Cardiology, Stuttgart, Germany; Karl Stangl, Charité CCM, Dept of Cardiology, Berlin, Germany; Michael Böhm, Univ Hosp Saarland, Dept of Cardiology, Homburg / Saar, Germany; Herbert Boll, Robert-Bosch-GmbH, Stuttgart, Germany; Götz Gelbrich, Universität Leipzig, KKS, Leipzig, Germany; Bridget-Ann Kirwan, SOCAR Resch SA, Nyon, Switzerland; Stefan D Anker, Charité CW, Dept of Cardiology, Berlin, Germany

Rationale: Remote patient management (telemedicine) may help to detect early signs of cardiac decompensation, allow to optimize therapy and improve treatment compliance in chronic heart failure (CHF). Two meta-analyses suggested that telemedicine in CHF can reduce mortality by 30–35%. We aimed to prospectively investigate the impact of telemedical management on mortality in ambulatory CHF patients. Design: CHF patients (NYHA II/III, LVEF ≤ 50% with a history of cardiac decompensation with hospitalization in the past 18 months (no hospitalization required if LVEF ≤ 25%), were randomized 1:1 to an intervention group of daily remote device monitoring (ECG, blood pressure, body weight) coupled with medical telephone support or to usual care lead by the patients local physician. In the intervention group 24/7 physician led medical support was provided by 2 central telemedical centers (located in Berlin and Stuttgart); Methods: We recruited ambulatory patients in 3 areas of varying economic status in Germany (Berlin, Brandenburg and Baden-Württemberg). A clinical event committee blinded to treatment allocation assessed cause of death and reason for hospitalization. Primary endpoint: total mortality; first secondary endpoint: composite of cardiovascular mortality or hospitalization due to heart failure; other secondary endpoints included cardiovascular mortality, all-cause and cause-specific hospitalizations (all time to first event) as well as days lost due to heart failure hospitalization or cardiovascular death (n % of follow-up time), and quality of life and NYHA class at 12 months. Results: Overall, 710 CHF patients were recruited. The follow-up was at least 12 months in all patients (mean 24.3 ± 5.1 months) and overall amounted to 1437 patient-years. Survival information will be available for all patients. Baseline details of all patients: age 67 ± 11 yrs, female gender 19%, LVEF 27 ± 6%, NYHA class III 50%, ACEi/ARB treatment 95%, beta-blocker treatment 92%, diuretics 92%, ICD therapy 46%. Conclusion: This study will provide information on the efficacy of telemedical 24/7 physician led support in CHF patients with systolic dysfunction over a mean follow-up of 24 months. Results of TIM-HF will be available by September 2010 and will be presented.

Author Disclosures: F. Köhler: None; S. Winkler: None; M. Schieber: None; U. Sechtem: None; K. Stangl: None; M. Böhm: None; H. Boll: Employment; Significant; BOSCH AG; G. Gelbrich: None; B. Kirwan: SOCAR Research SA; S.D. Anker: Consultant/Advisory Board; Significant; BOSCH AG.
The Resuscitation Outcomes Consortium ROC PRIMED Impedance Threshold Device and Active Compression Decompression Cardiopulmonary Resuscitation: A Prospective, Randomized, Double-Blind, Controlled Clinical Trial

Tom P Aufderheide, Med College of Wisconsin, Milwaukee, WI; Graham Nichol, Thomas D Rea, Univ of Washington-Harborview Ctr for Prehospital Emergency Care, Seattle, WA; Sohshan Everson-Stewart, Brian Leroux, Univ of Washington Clinical Trial Ctr, Seattle, WA; Peter J Kudenchuk, Univ of Washington-Harborview Ctr for Prehospital Emergency Care, Seattle, WA; Jeff Christenson, Univ of British Columbia, Vancouver, BC, Canada; Paul E Pepe, UT Southwestern Med Ctr, Dallas, TX; Tom P Aufderheide, Oregon Health Sciences Univ, Portland, OR; Paul Dorian, Univ of Toronto, Toronto, ON, Canada; Clifford W Callaway, Univ of Pittsburgh, Pittsburgh, PA; Ahmed H Idris, UT Southwestern Med Ctr, Dallas, TX; Douglas Andrusiek, British Columbia Emergency & Health Svs Commission, Vancouver, BC, Canada; Shannon W Stephens, Univ of Alabama at Birmingham, Birmingham, AL; David Hostler, Univ of Pittsburgh, Pittsburgh, PA; Daniel P Davis, James V Dunford, Univ of California, San Diego, CA; Ronald G Pirrello, Medical Coll of Wisconsin, Milwaukee, WI; Ian G Stiel, Catherine M Clement, Univ of Ottawa, Ottawa, ON, Canada; Alan Craig, Brigham Emergency Medical Svcs, Toronto, ON, Canada; Luis Van Ottingham, University of Washington Clinical Trial Ctr, Seattle, WA; Terri A Schmidt, Oregon Health Sciences Univ, Portland, OR; Henry Wang, Univ of Alabama at Birmingham, Birmingham, AL; Myron L Weissfeld, Johns Hopkins Sch of Medicine, Baltimore, MD; Joseph P Ornato, NHLBI, NIH, Rockville, MD; and the Resuscitation Outcomes Consortium (ROC) Investigators

Background: Previous studies suggest use of the impedance threshold device (ITD) during CPR may improve survival for victims of cardiac arrest. We compared survival to hospital discharge with the modified Rankin score of ≤3 in patients undergoing manual chest compressions and cardiopulmonary resuscitation (CPR) with a sham or active ITD.

Methods: This prospective, multi-center, double-blind, randomized, controlled, clinical trial evaluated adult patients (≥18 years old or local age of consent) with non-traumatic out-of-hospital cardiac arrest treated by emergency medical services (EMS) in the Resuscitation Outcomes Consortium. A partial factorial design was implemented concurrently entering patients with initially 30 seconds of chest compressions (Analyze Early) versus 3 minutes of chest compressions (Analyze Later).

Results: There were 8,718 evaluable patients enrolled in the study. 4,345 (49.9%) of patients were treated with a sham ITD and 4,373 (50.2%) with an active ITD. Patient demographics, cardiac arrest location, incidence of bystander CPR, and time to EMS arrival were similar between groups. The overall number and proportion of patients who survived to hospital discharge with a modified Rankin score of ≤3 was 262/3435 (7.6%) with a sham ITD and 254/3437 (7.4%) with an active ITD, p = 0.61. There were no statistically significant differences in pre-specified subgroup analyses or safety measures.

Conclusion: In this large effectiveness trial, manual chest compressions and an active ITD did not significantly improve functional survival from cardiac arrest compared with a sham ITD.


Treatment of Out-of-Hospital Cardiac Arrest with an Impedance Threshold Device and Active Compression Decompression Cardiopulmonary Resuscitation Improves Survival with Good Neurologic Function: Results from the RESQTrial

Tom P Aufderheide, Medical Coll of Wisconsin, Milwaukee, WI; Ralph J Frascone, Marvin A Brian, D Mahoney, Regions Hosp Emergency Med Services, Oakland, MN; Robert A Swor, Wm. Beaumont Hosp, Royal Oak, Mi; Robert M Demeure, Michael L Olinger, Richard G Holcomb, David E Tupper, Regions Hosp Emergency Med Services, Oakland, MN; Demetris Yannopoulos, Johns Hopkins Univ, Baltimore, MD; Keith G Lurie; Univ of Minnesota Health Ctr, Minneapolis, MN

Background: Adding an impedance threshold device (ITD) to active compression decompression cardiopulmonary resuscitation (ACD-CPR) decreases intrathoracic pressure during the decompression phase of CPR, improving hemodynamics. We hypothesized that ITD + ACD-CPR would increase survival with good neurologic function after out-of-hospital cardiac arrest (OHCA).

Methods: This prospective, randomized, multicenter trial evaluated adults with OHCA treated by emergency medical services (EMS) in seven study sites in the United States, encompassing a population of 2.3 million. Patients were assigned to ITD + ACD-CPR (intervention) or standard CPR (control) on a 1:1 proportional basis. CPR was initiated by the first arriving basic or advanced life support EMS provider. The primary endpoint was survival to hospital discharge with good neurologic function, defined as a modified Rankin Score (MRS) ≤3.

Results: Inclusions included events with neurologic outcome occurring during the Cerebral Performance Category (CPC). Patients meeting final criteria (non-traumatic arrest, presumed cardiac etiology) were included in the primary intent-to-treat analysis.

HT1-303 The Trauma Formula-driven versus Laboratory-Guided Study: Challenges and Lessons in Designing a Massive Transfusion Randomized Control Trial in Trauma

Sandro Rizoli, Bartolomeu Nascimento, Homer Tien, Yuila Lin, Jennie Callum; Univ of Toronto, Toronto, ON, Canada

Background: About 25 % of all severely traumatized patients are coagulopathic on arrival to hospital, where bleeding remains the first cause of death. A novel strategy proposes addressing coagulopathy and resuscitating multiple bleeding patients (1 per 1 ml blood cell transfusion = 1 plasma + 1 platelet). Initial clinical results are encouraging but come from retrospective studies with major limitations. This is the first prospective randomized controlled trial (RCT) on the topic and compares 1:1:1 formula with conventional laboratory-guided resuscitation. This preliminary analysis reports the challenges of this feasibility RCT. Methods: Adults with blunt or penetrating trauma, hypotensive, bleeding and potentially requiring massive transfusion are randomized (under delayed informed consent) to either laboratory-guided or 1:1:1 formula. Interventions are applied up to 12h post-trauma and/or bleeding stops. Blood products are continuously released in 1:1:1 ratio for the formula group and no laboratory tests are required. For the conventional control group, blood transfusions are guided by laboratory, products are continuously released in 1:1:1 ratio for the formula group and no laboratory tests are required. For the conventional control group, blood transfusions are guided by laboratory tests or point-of-care testing. Early endpoints were missed for failure to activate the research team. Median (interquartile range) time to death was 20, 43 and 41/min with 1/3 of TAT spent on transporting samples. Conclusion: Major challenges and strategies to implement massive transfusion protocols and randomize unstable patients were identified. The feasibility of conducting such a massive transfusion study relies mostly on prompt activation of research personnel (currently triggered by uncrossmatched blood request); simple inclusion criteria; Data Monitoring Board for post-randomization exclusions; readily available thawed plasma or fast thawing method (microwaves); delayed consent and fast TAT for laboratory tests or point-of-care testing.

This randomized trial was conducted over one year. Nursing students (n=606) completed either HeartCode™ BLS or an instructor-led course and were then randomly assigned to an experimental (6 minutes of practice/month on a voice advisory manikin) or control (no practice) group. Every 3 months, a subset of students was randomly selected from both groups for reassessment of their CPR skills. Once students were assessed at any given time point, their participation ended because the assessment, in effect, served as an additional practice session. Results: Based on compression depth and ventilation rate and volume, the intervention group performed better than the control over the 12 months and, in some parameters, showed steady improvement over time. In the control group, students lost their ability to compress with adequate depth between 9 and 12 months (p<0.004) and to ventilate with an adequate volume by 3 months (p<0.0001) after their initial CPR training. Conclusions: The findings of this study not only confirmed the importance of practicing CPR psychomotor skills to retain them but also revealed that short monthly practices can improve skills over baseline. The results also demonstrated that self-directed CPR skills practice on a manikin with some form of automated feedback was a viable option for delivering frequent practice sessions to nursing students and, potentially, to practicing nursing staff and other health care providers.

Author Disclosures: M.H. Oermann: Research Grant; Modest; Laerdal Medical Corp. Other Research Support; Modest; Laerdal Medical Corp. S.E. Kardong-Edgren: None. T. Odom-Maryon: None.

HTS-305
Resuscitation Outcomes Consortium ROC PRIMED Trial of Early Rhythm Analysis versus Later Analysis in Out-of-Hospital Cardiac Arrest

Ian G Steil, Univ of Ottawa, Ottawa, ON, Canada; Graham Nichol, Univ of Washington-Harborview Ctr for Prehospital Emergency Care, Seattle, WA; Brian G. Leroux, Univ of Washington, Seattle, WA; Thomas D. Reis, Univ of Washington-Harborview Ctr for Prehospital Emergency Care, Seattle, WA; Joseph P Ornato, Virginia Commonwealth Univ, Richmond, VA; Judy Powell, Univ of Washington, Seattle, WA; James Christenson, Univ of British Columbia, Vancouver, BC, Canada; Clifford W Callaway, Univ of Pittsburgh, Pittsburgh, PA; Peter J Kudenchuk, Univ of Washington, Seattle, WA; Tom P Aufderheide, Medical Coll of Wisconsin, Milwaukee, WI; Ahamed H Idries, Univ of Texas Southwestern Med Cntr, Dallas, TX; Mohammad Daya, Oregon Health & Science Univ, Portland, OR; Henry E Wang, Univ of Alabama at Birmingham, Birmingham, AL; Laurie Morrison, Univ of Toronto, Toronto, ON, Canada; Daniel Davis, Univ of California, San Diego, CA; Dug Andrusiek, Univ of British Columbia, Vancouver, BC, Canada; Shannon Stephens, Univ of Alabama at Birmingham, Birmingham, AL; Sheldon Cheskes, Univ of Toronto, Toronto, ON, Canada; Robert H Schmicker, Univ of Washington, Seattle, WA; Ray Fowler, Univ of Texas Southwestern Med Cntr at Dallas, Dallas, TX; Christian Vaillancourt, Univ of Ottawa, Ottawa, ON, Canada; David Hostier, Univ of Pittsburgh, Pittsburgh, PA; Dana Zive, Oregon Health & Science Univ, Portland, OR; Ronald G Pirralo, Med College of Wisconsin, Milwaukee, WI; Gary Vilke, Univ of California, San Diego, CA; George Sopko, NHLBI, NIH, Rockville, MD; Myron Weisfeld, Johns Hopkins Med Insts, Baltimore, MD; and the Resuscitation Outcomes Consortium (ROC) Investigators

Background: In a departure from the prior immediate defibrillation paradigm, the 2005 AHA/ILCOR resuscitation guidelines recommended that Emergency Medical Service (EMS) rescuers could provide two minutes of cardiopulmonary resuscitation (CPR) before cardiac rhythm analysis. We compared brief CPR with early analysis versus longer CPR with delayed analysis. Methods: We conducted a cluster randomized crossover trial of adult out-of-hospital cardiac arrests (OOHCA) patients at 10 Resuscitation Outcomes Consortium sites in the U.S. and Canada. Patients in the Analyze Early group were allocated to receive 30–60 seconds of EMS CPR and those in the Analyze Later group were allocated to receive 180 seconds of CPR before initial ECG analysis. Results: We enrolled 9,934 patients. The primary outcome, survival to hospital discharge with satisfactory function (Modified Rankin Scale score ≤ 3), did not differ between the Analyze Early and Later groups (5.9% versus 5.9%, P=0.91) with a cluster-adjusted absolute difference of −0.2% (95% CI −1.1% to 0.7%). Analyses adjusted for confounders and a priori and post-hoc subgroup analyses showed no survival benefit for either study group. Exploratory analyses suggest that with the passage of time to first ECG analysis, survival does not improve, whereas for VF/VT patients with bystander CPR, survival may even tend to decline. Conclusions: For OOHCA we found no difference in outcomes between a brief as compared with longer period of EMS CPR before the first rhythm analysis. Our findings suggest the AHA/ILCOR recommendation permitting two minutes of EMS CPR before analysis is unlikely to provide greater benefit than CPR of shorter duration.

2010 Clinical Trial/Clinical Science Abstracts

Circulation. 2010;122:2215-2226
doi: 10.1161/CIR.0b013e318200c0b5
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2010 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the
World Wide Web at:
http://circ.ahajournals.org/content/122/21/2215

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation is online at:
http://circ.ahajournals.org/subscriptions/