Summaries of Key Journal Articles

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Arrhythmias

Early Versus Later Rhythm Analysis in Patients With Out-of-Hospital Cardiac Arrest


Study Question: Is survival after out-of-hospital cardiac arrest (OHCA) affected by the duration of manual cardiopulmonary resuscitation (CPR) before initial rhythm analysis?

Methods: This prospective study was performed by the Resuscitation Outcomes Consortium in 9,933 patients (mean age 67 years) with OHCA. Upon arrival of emergency medical services (EMS), the patients were randomly assigned to early rhythm analysis (30-60 seconds of CPR before rhythm analysis, n = 5,290) or delayed rhythm analysis (180 seconds of CPR before rhythm analysis, n = 4,643). The primary outcome was survival to hospital discharge with satisfactory functional status.

Results: The median time to rhythm analysis was 42 seconds in the early-analysis group and 180 seconds in the later-analysis group. Survival to hospital discharge with satisfactory functional status was 5.9% in both groups.

Conclusions: Survival after OHCA is not improved by lengthening the amount of EMS-administered CPR from 30-60 seconds to 180 seconds before rhythm analysis.

Perspective: Some prior experimental and clinical studies have demonstrated improved outcomes after OHCA when CPR is performed for 3 minutes before rhythm analysis (and defibrillation if appropriate). This study provides strong evidence against a beneficial effect of additional CPR before initial rhythm analysis. The results suggest that there is no reason to defer rhythm analysis and defibrillation once the chest electrodes are in place.

Summary written by: Fred Morady, MD

Reversal of Rivaroxaban and Dabigatran by Prothrombin Complex Concentrate: A Randomized, Placebo-Controlled, Crossover Study in Healthy Subjects

Eerenberg ES, Kamphuisen PW, Sijpkens MK, Meijers JC, Buller HR, Levi M. Circulation 2011;Sep 6:[Epub ahead of print].

Study Question: What is the potential of prothrombin complex concentrate (PCC) to reverse the anticoagulant effect of rivaroxaban or dabigatran?

Methods: The authors reported the results of a randomized, double-blind, placebo-controlled, crossover trial in 12 healthy male subjects receiving rivaroxaban 20 mg twice daily (n = 6) or dabigatran 150 mg twice daily (n = 6) for 2.5 days, followed by either a single bolus of 50 IU/kg PCC (Cofact) or a similar volume of saline. After a washout period of 11 days, the groups were crossed over, and the
protocol repeated. Anticoagulant effect of rivaroxaban was assessed with prothrombin time (PT) and thrombin generation, as measured by the endogenous thrombin potential (ETP). Dabigatran effect was measured by activated partial thromboplastin time (aPTT), ecarin clotting time (ECT), and thrombin time (TT).

**Results:** PT was prolonged by rivaroxaban (15.8 ± 1.3 vs. 12.3 ± 0.7 seconds at baseline; p < 0.001) that was immediately reversed by PCC (12.8 ± 1.0; p < 0.001). ETP was inhibited by rivaroxaban (51 ± 22%; baseline, 92 ± 22%; p = 0.002) and normalized with PCC (114 ± 26%; p < 0.001). No effect was seen with saline placebo. There was a significant, immediate increase in aPTT, ECT, and TT by dabigatran. PCC had little effect on these parameters after dabigatran.

**Conclusions:** PCC immediately and completely reverses the anticoagulant effect of rivaroxaban in healthy subjects, but has no influence on the anticoagulant action of dabigatran at the PCC dose used in this study.

**Perspective:** This important study is a systematic attempt to answer an essential question regarding the two newest Food and Drug Administration (FDA) approved anticoagulants for clinical use in this country. As these agents are rapidly adopted for clinical use, and indications approved by the FDA expand, the need to assess and reverse their effect will be increasingly important. At this point, highly effective solutions are identified for rivaroxaban, while dabigatran remains without any identified reversal agent. Further evaluation is needed, given the widespread indications for these agents.

*Summary written by: James B. Froeblich, MD, MPH*

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**Cardiovascular Surgery**

**Do Bad Report Cards Have Consequences? Impacts of Publicly Reported Provider Quality Information on the CABG Market in Pennsylvania**


**Study Question:** What is the impact of coronary artery bypass grafting (CABG) report cards on a provider’s aggregate volume and volume by patient severity?

**Methods:** The investigators employed four different data sets in this study. The primary data are the Pennsylvania Inpatient Hospital Discharge Data collected by the Pennsylvania Health Care Cost Containment Council (PHC4). This data set contains clinical and utilization information at the patient level. Data elements include patients’ race/ethnicity, gender, age, zip code of residence, severity of illness, insurance type, the type of admission, the quarter of admission, the principal diagnosis code and secondary diagnoses codes, the principal procedure code and secondary procedure codes, discharge status, a four-digit unique facility identifier, and the license number of the operating physician. To test the effects of report cards on hospital-level volume, the authors use the number of CABG procedures performed in a hospital in a quarter as the dependent variable. They use regression equation using the number of CABG procedures performed by a surgeon in a quarter as the dependent variable to test the effects of report cards on surgeon-level volume.

**Results:** The results suggest that being identified as a high-mortality hospital in the most recent report card is associated with a decline of nine CABG surgeries per quarter. This decline is not statistically significant. For all CABG cases, being identified as a high-mortality surgeon was associated with a decline of 4.76 CABG surgeries per quarter, and the coefficient was significant at the 1% level. Being identified as a low-mortality surgeon was associated with an increase of 4.63 CABG surgeries per quarter, though this coefficient was not precisely estimated.

**Conclusions:** The authors found a reduction in volume of poor performing and unrated surgeons’ volume, but no effect on more highly rated surgeons or hospitals of any report card rating.

**Perspective:** The study reports that public reporting led to a decrease in volume for unrated and poor performing surgeons, but interestingly, the volume of the high performing surgeons does not increase by an offsetting amount. Results of the patient choice modeling suggest that public reporting leads to avoidance of poor performing or unrated surgeons. Additional research is needed to assess the degree to which report cards affect total welfare, as well as examining the mechanisms by which the report cards lead to the sorting and avoidance behavior reported in this study.

*Summary written by: Debabrata Mukherjee, MD*

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**Incidence of Aortic Complications in Patients With Bicuspid Aortic Valves**


**Study Question:** What is the incidence of aortic complications in patients with bicuspid aortic valve (BAV), in a community cohort and in the general population?

**Methods:** The investigators conducted a comprehensive assessment of aortic complications of patients with BAV living in a population-based setting in Olmsted County, MN. They analyzed long-term follow-up of a cohort of all Olmsted County residents diagnosed with definite BAV by echocardiography from 1980 to 1999, and searched for aortic complications of patients whose bicuspid valves had gone
undiagnosed. The last year of follow-up was 2008–2009. The main outcome measures were thoracic aortic dissection, ascending aortic aneurysm, and aortic surgery.

**Results:** The cohort included 416 consecutive patients with definite BAV, mean follow-up of 16 years (6,530 patient-years). Aortic dissection occurred in 2 of 416 patients; incidence of 3.1 cases per 10,000 patient-years, age-adjusted relative-risk 8.4 compared with the county’s general population. Aortic dissection incidences for patients 50 years or older at baseline and bearers of aortic aneurysms at baseline were 17.4 and 44.9 cases per 10,000 patient-years, respectively. Comprehensive search for aortic dissections in undiagnosed bicuspid valves revealed two additional patients, allowing estimation of aortic dissection incidence in bicuspid valve patients irrespective of diagnosis status, which was similar to the diagnosed cohort. Of 384 patients without baseline aneurysms, 49 developed aneurysms at follow-up, incidence of 84.9 cases per 10,000 patient-years and an age-adjusted relative risk 86.2. The 25-year rate of aortic surgery was 25%.

**Conclusions:** In the population of patients with BAV, the incidence of aortic dissection over a mean of 16 years of follow-up was low, but significantly higher than in the general population.

**Perspective:** This study suggests that patients with BAV develop a clinical aortopathy that affects clinical outcome. The dissection incidence was higher in patients older than 50 years and higher in those with baseline aortic aneurysms, highlighting the importance of close monitoring and implementation of current guidelines in these subgroups. Future research should focus on elucidating biological pathways of BAV aortopathy amenable to medical treatment, as well as identifying novel markers for refining risk prediction of aortic dissection in these patients.

*Summary written by:* Debabrata Mukherjee, MD

### General Cardiology

**Evaluation of C-Reactive Protein Prior to and On-Treatment as a Predictor of Benefit From Atorvastatin: Observations From the Anglo-Scandinavian Cardiac Outcomes Trial**

Sever PS, Poulter NR, Chang L, et al., on behalf of the ASCOT Investigators. *Eur Heart J* 2011; Jul 28:[Epub ahead of print].

**Study Question:** Among subjects enrolled in the ASCOT trial, was C-reactive protein (CRP) associated with increased risk of cardiovascular outcomes?

**Methods:** ASCOT enrolled subjects with total cholesterol levels ≥250 mg/dl, who were then randomized to atorvastatin (10 mg/day) or placebo. All subjects had a diagnosis of hypertension and three or more additional cardiovascular disease (CVD) risk factors. At baseline, participants had no history of myocardial infarction or currently treated angina. This was a case-controlled study of 485 CVD cases that were matched by age, sex, and study entry time, to 1,367 controls.

**Results:** Over a median follow-up of 5.5 years, 1,852 subjects were eligible for inclusion in this current analysis; 131 were excluded for missing values. The mean age was 64.7 years, and 84.7% were male. Baseline low-density lipoprotein (LDL) levels and log-transformed CRP were predictive of CVD events (odds ratio [OR], 1.31). Inclusion of CRP into the Framingham risk model improved risk prediction modestly. There was no evidence of an interaction between LDL and CRP and treatment effect on CVD events. A 6-month on-treatment LDL among those randomized to atorvastatin was associated with a significant reduction in CVD events (OR, 0.41). In contrast, CRP below the median (1.83 mg/L) compared with CRP above the median was not associated with a significant reduction in CVD events (OR, 0.86).

**Conclusions:** Among hypertensive patients with additional CVD risk factors, CRP did not improve prediction of events in a clinically meaningful way. Reduction in CRP associated with statin therapy was not a predictor of CVD outcomes alone or in combination with LDL levels.

**Perspective:** This is an interesting finding. Using data from ASCOT, these results support the continued use of traditional risk factors as a means of identifying patients at increased risk for CVD outcomes.

*Summary written by:* Elizabeth A. Jackson, MD


**Perspective:** The following are 10 points to remember from these European Society of Cardiology guidelines:

1. Acute coronary syndrome (ACS) is usually precipitated by acute thrombosis induced by a ruptured or eroded...
atherosclerotic coronary plaque, with or without concomitant vasoconstriction, causing a sudden and critical reduction in blood flow.

2: Blood has to be drawn promptly for troponin measurement. The result should be available within 60 minutes. The test should be repeated 6–9 hours after initial assessment if the first measurement is not conclusive. Repeat testing after 12–24 hours is advised if the clinical condition is still suggestive of ACS.

3: Angiography should be performed urgently for diagnostic purposes in patients at high risk and in whom the differential diagnosis is unclear. Coronary computed tomography angiography should be considered to exclude ACS when there is a low to intermediate likelihood of coronary artery disease, and when troponin and electrocardiogram are inconclusive.

4: Quantitative assessment of risk is useful for clinical decision making. The GRACE risk score provides the most accurate stratification of risk both on admission and at discharge.

5: Ticagrelor (180 mg loading dose, 90 mg twice daily) is recommended for all patients at moderate to high risk of ischemic events, regardless of initial treatment strategy and including those pretreated with clopidogrel.

6: Prasugrel (60 mg loading dose, 10 mg daily dose) is recommended for P2Y12-inhibitor-naïve patients in whom coronary anatomy is known and who are proceeding to percutaneous coronary intervention (PCI), unless there is a high risk of life-threatening bleeding or other contraindications.

7: Clopidogrel (300 mg loading dose, 75 mg daily dose) is recommended for patients who cannot receive ticagrelor or prasugrel.

8: Fondaparinux (2.5 mg subcutaneously daily) is recommended as having the most favorable efficacy–safety profile with respect to anticoagulation. If the initial anticoagulant is fondaparinux, a single bolus of unfractionated heparin (85 IU/kg adapted to activated clotting time) should be added at the time of PCI.

9: Urgent coronary angiography (<2 hours) is recommended in patients at very high ischemic risk (refractory angina, with associated heart failure, life-threatening ventricular arrhythmias, or hemodynamic instability).

10: Appropriate secondary prevention is of paramount importance since ischemic events continue to accrue at a high rate after the acute phase.

Summary written by: Debabrata Mukherjee, MD

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**Statins and Intracerebral Hemorrhage: A Retrospective Cohort Study**


**Study Question:** What is the association between statins and intracerebral hemorrhage (ICH) in patients with recent ischemic stroke in a population-based setting?

**Methods:** This was a retrospective propensity-matched cohort study with accrual from July 1, 1994 to March 31, 2008, in Ontario, Canada. A total of 17,872 patients ages 66 years and older who initiated statin therapy following acute ischemic stroke were followed for a median of 4.2 years. Main outcome measures were hospitalization or emergency department visit for ICH defined using validated diagnosis coding.

**Results:** Overall, 213 episodes of ICH occurred. In the primary analysis comparing statin users with nonusers, authors found no association between statins and ICH (hazard ratio, 0.87; 95% confidence interval, 0.65-1.17). Subgroup and dose-response analyses yielded similar results. In tests of specificity, statin therapy was not associated with bone mineral density testing, vitamin D or B12 screening, gastrointestinal endoscopy, or elective knee arthroplasty, suggesting that results were not due to healthy user bias or differences in quality of care.

**Conclusions:** Statin exposure following ischemic stroke was not associated with ICH.

**Perspective:** This study found no association between statins and subsequent ICH. This lack of harmful association was maintained across subgroup analyses, and irrespective of statin dosing. Based on these data and the meta-analysis of statin trials from the Cholesterol Treatment Trialists’ Collaboration, clinicians should continue to adhere to current national treatment guidelines recommending statin therapy for most patients with a history of ischemic stroke.

*Summary written by: Debabrata Mukherjee, MD*

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**Heart Failure/Transplant**

**Management of Chronic Heart Failure in Adults: Synopsis of the National Institute for Health and Clinical Excellence Guideline**


**Conclusions:** The following are points to remember about the management of chronic heart failure (HF) in adults:
1: The National Institute for Health and Clinical Excellence (NICE) develops clinical practice guidelines for the National Health Service of England and Wales. Based on literature searches (cut-off date, October 2009), the guidelines development group (GDG) of NICE made new recommendations for the diagnosis and management of HF.

2: Their studies found a net savings of £19,000 per 100,000 persons if all of these recommendations were implemented.

3: The American College of Cardiology Foundation/American Heart Association guidelines focus on the assessment of HF rather than determining whether a patient has this syndrome. The European Society of Cardiology guidelines on diagnosis recommend that all patients with symptoms suggestive of HF undergo echocardiography and measurement of serum natriuretic peptide levels, whereas NICE recommends discerning utilization of these diagnostic tests.

4: In diagnosis, the NICE guideline focuses on using both a history of myocardial infarction and an increase in serum natriuretic peptide levels to guide further assessment. It also recommends time limits within which patients should receive both echocardiography and clinical assessment by a specialist. Their review of the literature concluded that clinical signs and symptoms are of limited use in the diagnosis of HF, and that measurement of serum natriuretic peptide levels (both B-type natriuretic peptide [BNP] and N-terminal pro-BNP) has high sensitivity, but only moderate specificity for diagnosis of HF.

5: The GDG encourages increased use of beta-blockers and angiotensin-converting enzyme inhibitors as first-line therapy in patients with HF and left ventricular systolic dysfunction, and proposes options for second-line therapy (aldosterone antagonists, angiotensin-receptor blockers, or combination therapy with a nitrate and hydralazine).

Perspective: Clearly, the National Health Service has to allocate scarce resources and, hence, the NICE guidelines focus on what is cost-effective in the British system to diagnose and treat HF. For example, there is a limited pool of specialists and cardiologists in the UK and, therefore, often the management of milder HF has to be done by general practitioners. Therefore, these guidelines may be appropriate in the UK, where resource allocation has to be done in a measured fashion. However, the cumulative risk reduction if all of the three therapies (i.e., ACE inhibitors, beta-blockers, and aldosterone receptor blockers) are used was 63% and absolute risk reduction was 22%. Therefore, the number needed to treat = 5 (Fonarow G, et al., *Braunwald's Atlas of Heart Diseases*, Volume 15, Chapter 5, Current Medicine).

Summary written by: Ragavendra R. Baliga, MBBS

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**N-Terminal Pro-Brain Natriuretic Protein Levels in Takotsubo Cardiomyopathy**


**Study Question:** Do N-terminal probrain natriuretic peptide (NT-proBNP) levels correlate with inflammatory markers, catecholamines, and/or cardiopulmonary hemodynamics in takotsubo cardiomyopathy (TCC)?

**Methods:** Patients (n = 56) with TCC underwent echocardiography and laboratory assessment (NT-proBNP, troponin, C-reactive protein, normetenephrine levels) at baseline, 10 days, and 3 months after diagnosis. All patients underwent angiogram at baseline to exclude significant coronary disease; 34 had a right heart catheterization and 42 had cardiac magnetic resonance imaging on index presentation. Correlations between NT-proBNP, baseline wedge pressure, wall stress by MRI, and wall motion score index by echocardiogram were examined.

**Results:** The mean patient age was 69 years, 96% (n = 54) were female, and 81% had experienced an acute stressor in life. At baseline, mean left ventricular ejection fraction (LVEF) was 53 ± 13%, 100% had an elevation of troponin T (median 0.32), and 36% had ST elevation on admission electrocardiogram. Median baseline NT-proBNP level was 1325 pg/ml at presentation, and levels increased significantly (NT-proBNP 4382 pg/ml) within 24 hours of presentation, with a slow and incomplete normalization by 3 months. Median baseline plasma norepinephrine concentrations (998 pmol/L) were significantly correlated (r = 0.53, p = 0.001) with peak NT-proBNP levels. Correlations with C-reactive protein were weak (r = 0.3, p = 0.05). Likewise, NT-proBNP correlated with baseline LVEF (r = −0.39, 0.008) and the extent of impaired wall motion (r = 0.37, p = 0.008) found on echocardiogram.

**Conclusions:** TTC is associated with elevated NT-proBNP levels, and these levels correlate with catecholamine increases and decrements in LV systolic function.

**Perspective:** The authors provide interesting insight into TCC. By demonstrating that NT-proBNP continues to increase after admission, they suggest that the hormone increment is likely the result of increased synthesis rather than release of pre-formed peptides in response to catecholamine stress. Since catecholamine stress is associated with myocardial calcium toxicity and inflammation is a cardiac depressant, perhaps unmeasured extracellular and intracellular biochemical imbalances and perturbations are at play in this interesting disease.

Summary written by: Jennifer Ann Cowger, MD, MS
Interventional Cardiology

**Clopidogrel Pre-Treatment Is Associated With Reduced In-Hospital Mortality in Primary Percutaneous Coronary Intervention for Acute ST-Elevation Myocardial Infarction**

Dörler J, Edlinger M, Alber HF, et al., on behalf of the Austrian Acute PCI Investigators. 
Eur Heart J 2011; Sep 14: [Epub ahead of print].

**Study Question:** What is the clinical benefit of preloading with clopidogrel in patients undergoing primary percutaneous coronary intervention (PCI) for ST-segment elevation myocardial infarction (STEMI)?

**Methods:** The authors compared the outcome of patients pre-treated with clopidogrel (prior to arrival at the PCI center) with those who were not preloaded prior to undergoing primary PCI. All patients were enrolled in the Austrian Acute PCI registry.

**Results:** Of the 5,955 patients who underwent primary PCI, 1,635 patients were pretreated with clopidogrel. Patients pretreated with clopidogrel were less likely to be in cardiogenic shock (8.4% vs. 11.2%) or require cardiopulmonary resuscitation prior to PCI (5.2% vs. 9.6%). Clopidogrel pretreatment was associated with lower in-hospital mortality (3.4 vs. 6.1%, p < 0.01) after primary PCI. After adjusting for baseline differences, clopidogrel pretreatment was an independent predictor of lower in-hospital mortality. This difference was more pronounced in the patients who were treated with platelet glycoprotein IIb/IIIa inhibitors in the catheterization laboratory.

**Conclusions:** Clopidogrel pretreatment is associated with a lower mortality among patients undergoing primary PCI for STEMI.

**Perspective:** This study suggests that clopidogrel preloading is associated with a dramatic reduction in in-hospital mortality among patients undergoing primary PCI. Clopidogrel preloading was more commonly performed in patients who were less sick, and it is not clear if the findings of this study reflect immigration bias and residual confounding or a true survival benefit of early clopidogrel.

*Summary written by: Hitinder S. Gurm, MBBS*

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**Stenting Versus Aggressive Medical Therapy for Intracranial Arterial Stenosis**

Chimowitz MI, Lynn MJ, Derdeyn CP, et al., on behalf of the SAMMPRIS Trial Investigators.
N Engl J Med 2011; Sep 7: [Epub ahead of print].

**Study Question:** What is the role of percutaneous transluminal angioplasty and stenting (PTAS) for intracranial arterial stenosis?

**Methods:** The investigators randomly assigned patients who had a recent transient ischemic attack or stroke attributed to stenosis of 70-99% of the diameter of a major intracranial artery to aggressive medical management alone, or aggressive medical management plus PTAS with the use of the Wingspan stent system. The primary endpoint was stroke or death within 30 days after enrollment or after a revascularization procedure for the qualifying lesion during follow-up, or stroke in the territory of the qualifying artery beyond 30 days.

**Results:** Enrollment was stopped after 451 patients underwent randomization, because the 30-day rate of stroke or death was 14.7% in the PTAS group (nonfatal stroke, 12.5%; fatal stroke, 2.2%) and 5.8% in the medical-management group (nonfatal stroke, 5.3%; non–stroke-related death, 0.4%). Beyond 30 days, stroke in the same territory occurred in 13 patients in each group. The mean duration of follow-up, which is ongoing, is 11.9 months. The probability of the occurrence of a primary endpoint event over time differed significantly between the two treatment groups (p = 0.009), with 1-year rates of the primary endpoint of 20.0% in the PTAS group and 12.2% in the medical-management group.

**Conclusions:** In patients with intracranial arterial stenosis, aggressive medical management was superior to PTAS.

**Perspective:** This study suggests that aggressive medical therapy was superior to PTAS in high-risk patients with intracranial stenosis, because the rate of periprocedural stroke after PTAS was higher than expected and the rate of stroke in the medical-management group was lower than estimated. Essential elements of the aggressive medical regimen used in this trial can readily be adopted in clinical practice, including adding clopidogrel to aspirin for the first 90 days and lowering blood pressure and low-density lipoprotein cholesterol to achieve target levels based on national guidelines.

*Summary written by: Debabrata Mukherjee, MD*
Prevention/Vascular

High Residual Platelet Reactivity After Clopidogrel Loading and Long-Term Cardiovascular Events Among Patients With Acute Coronary Syndromes Undergoing PCI


Study Question: Is high residual platelet reactivity (HRPR) an independent prognostic marker of risk of long-term thrombotic events in patients with acute coronary syndromes (ACS) undergoing an invasive procedure?

Methods: This was a prospective, observational, referral center cohort study of 1,789 consecutive patients with ACS undergoing percutaneous coronary intervention (PCI) from April 2005 to April 2009, at the Division of Cardiology of Careggi Hospital, Florence, Italy, in whom platelet reactivity was prospectively assessed by light transmittance aggregometry. All patients received 325 mg of aspirin and a loading dose of 600 mg of clopidogrel, followed by a maintenance dosage of 325 mg/d of aspirin and 75 mg/d of clopidogrel for at least 6 months. Patients with HRPR, as assessed by adenosine diphosphate (ADP) test (≥70% platelet aggregation), received an increased dose of clopidogrel (150-300 mg/d) or switched to ticlopidine (500-1000 mg/d) under ADP test guidance. The primary endpoint was a composite of cardiac death, myocardial infarction, any urgent coronary revascularization, and stroke at 2-year follow-up. Secondary endpoints were stent thrombosis and each component of the primary endpoint.

Results: The primary endpoint event rate was 14.6% (36/247) in patients with HRPR and 8.7% (132/1,525) in patients with low residual platelet reactivity. Stent thrombosis was higher in the HRPR group compared with the low residual platelet reactivity group (6.1% vs. 2.9%). By multivariable analysis, HRPR was independently associated with the primary endpoint and with cardiac mortality.

Conclusions: Among patients receiving platelet reactivity–guided antithrombotic medication after PCI, HRPR status was significantly associated with increased risk of ischemic events at short- and long-term follow-up.

Perspective: This study also suggests that normalization of the ADP test result after treatment adjustment is not associated with better outcome versus a persistent abnormal ADP test result. It remains to be seen if HRPR after 600 mg clopidogrel loading in patients undergoing PCI for ACS is a non-modifiable risk factor for thrombotic events or if tailored therapy with use of newer, more potent antithrombotic agents such as prasugrel or ticagrelor may have a beneficial effect on clinical outcome in these patients.

Summary written by: Debabrata Mukherjee, MD

General and Abdominal Obesity and Risk of Death Among Black Women


Study Question: What is the relation of general and abdominal obesity to the risk of death in black women?

Methods: The investigators prospectively assessed the relation of both body mass index (BMI) and waist circumference to the risk of death among 51,695 black women with no history of cancer or cardiovascular disease who were 21-69 years of age at study enrollment. Their analysis was based on follow-up data from 1995 through 2008 in the Black Women’s Health Study.

Results: Of 1,773 deaths identified during follow-up, 770 occurred among 33,916 women who had never smoked. Among nonsmokers, the risk of death was lowest for a BMI of 20.0-24.9. For a BMI above this range, the risk of death increased as the BMI increased. With a BMI of 22.5-24.9 as the reference category, multivariable-adjusted hazard ratios were 1.12 for a BMI of 25.0-27.4, 1.31 for a BMI of 27.5-29.9, 1.27 for a BMI of 30.0-34.9, 1.51 for a BMI of 35.0-39.9, and 2.19 for a BMI of 40.0-49.9 (p < 0.001 for trend). A large waist circumference was associated with an increased risk of death from any cause among women with a BMI of <30.0.

Conclusions: The risk of death from any cause among black women increased with an increasing BMI of 25.0 or higher.

Perspective: This large prospective study suggests that the risk of death from any cause among black women was lowest among women with a BMI of 20.0-24.9, with an increased risk of death for all categories of BMI in the overweight and obesity range. A larger waist circumference was associated with an increase in the risk of death from any cause only among nonobese nonsmokers. Future studies will need to assess the survival advantage conferred on those individuals who lose weight.

Summary written by: Debabrata Mukherjee, MD
Meta-Analysis Comparing Mediterranean to Low-Fat Diets for Modification of Cardiovascular Risk Factors


Study Question: What is the relative value of a Mediterranean diet compared to low-fat diets for modifying cardiovascular risk factors?

Methods: MEDLINE, EMBASE, Biosis, Web of Science, and the Cochrane Central Register of Controlled Trials were searched from their inception until January 2011. Additionally, experts in the field were asked to identify randomized controlled trials (RCTs) comparing Mediterranean to low-fat diets in overweight/obese individuals, with a minimum follow-up of 6 months, reporting intention-to-treat data on cardiovascular risk factors. Two authors independently assessed trial eligibility and quality.

Results: Six RCTs were identified that included 2,650 individuals (50% women). Mean age of enrolled patients ranged from 35 to 68 years, and mean body mass index from 29 to 35 kg/m². After 2 years of follow-up, individuals assigned to a Mediterranean diet had more favorable changes in weighted mean differences of body weight (-2.2 kg), body mass index (-0.6 kg/m²), systolic blood pressure (-1.7 mm Hg), diastolic blood pressure (-1.5 mm Hg), fasting plasma glucose (-3.8 mg/dl), total cholesterol (-7.4 mg/dl), and high-sensitivity C-reactive protein (-1.0 mg/L). The observed heterogeneity across individual trials could be eliminated by restricting analyses to trials with balanced co-interventions or trials with restriction of daily calorie intake in both diet groups.

Conclusions: Mediterranean diets appear to be more effective than low-fat diets in inducing clinically relevant long-term changes in cardiovascular risk factors and inflammatory markers.

Perspective: The observed differences for the individual risk factors were modest, but would be meaningful in large cohorts. The Lyon Diet-Heart Study (not included) found a 70% reduction in overall mortality with the Mediterranean diet when compared to standard post-event diet recommendations in survivors of a myocardial infarction. The Mediterranean diet was posited to be of value when the risk of cardiovascular events was found to be low in men from the island of Crete. The contents of value include high fiber, fruits and vegetables, fish, and wine.

Summary written by: Melvyn Rubenfire, MD

Effects of a Home-Based Walking Intervention on Mobility and Quality of Life in People With Diabetes and Peripheral Arterial Disease: A Randomized, Controlled Trial


Study Question: What is the efficacy of a home-based walking intervention to improve walking ability and quality of life in people with diabetes and peripheral arterial disease (PAD)?

Methods: This was a multisite controlled, single-blind trial in which 145 patients (45 women) with diabetes and PAD were randomized to the intervention (a 6-month behavioral intervention targeting levels of readiness to engage in routine walking for exercise) versus attention control. Primary outcome was 6-month change in maximal treadmill walking distance. Secondary outcomes included 3-month change in maximal walking distance, lower limb function (i.e., walking impairment scores), quality of life (Medical Outcomes Short Form Survey), exercise behaviors, depressive symptoms, and self-efficacy at 3 and 6 months.

Results: The mean age of participants was 66.5 years. Intervention and control groups did not differ significantly in 6-month change in maximal treadmill walking distance (average 24.5 m vs. 39.2 m; p = 0.60). Among secondary outcomes, for the intervention and control groups, respectively, average walking speed scores increased by 5.7 units and decreased by 1.9 units (p = 0.03); the mental health quality of life subscale score increased by 3.2 and decreased by 2.4 units (p = 0.01).

Conclusions: A home-based walking intervention did not improve walking distance, but did improve walking speed and quality of life in people with diabetes and PAD. Clinicians should consider recommending home-based walking therapy for such patients.

Perspective: While the results are disappointing, the improvement in walking speed and quality of life are impressive, considering that all the patients were diabetics. The program included counseling for exercise intervention, two walking training sessions with an instructor, and individual and group walking in the community. This would be considerably less costly compared to onsite supervised PAD rehabilitation.

Summary written by: Melvyn Rubenfire, MD

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