Characteristics of Thoracic Aortic Aneurysm

Thoracic Aortic Aneurysm: Clinically Pertinent Controversies and Uncertainties.

Elefteriades JA, Farkas EA:

J Am Coll Cardiol 2010; 55 (March 2): 841-857

Ascending aortic aneurysms are non-arteriosclerotic, grow gradually in size, and are often familial.

This excellent state-of-the-art paper discusses current understanding of thoracic aortic aneurysms with a clinical focus. The take-home points are as follows: (1) It is important to avoid errors when measuring aortic dimensions, recognizing that variations of <3 to 4 mm may just reflect limited resolution of the imaging modality used. As the aorta enlarges in the thoracic cavity, it becomes tortuous; thus axial imaging planes may slice the aorta obliquely, thereby overestimating the aortic size. (2) Aortic aneurysms enlarge gradually (1 mm/year); thus it is important to compare the very first imaging study with the most recent in order to accurately detect enlargement. The authors note that the only instance that an aneurysm will expand abruptly is if it dissects; thus large changes in reported diameter over a short time usually reflect measurement error. (3) 6-cm dilation for the ascending aorta and 7-cm dilation for the descending aorta are important “hinge points” when aortic wall stress is the highest and compliance is the lowest, beyond which the risk of rupture increases dramatically. Thus 5.5 cm is the recommended size for repair of asymptomatic ascending aortic aneurysms. This dimension is 5 cm in those with Marfan's syndrome, bicuspid aortic valve, or family history of aortic disease. (4) Symptomatic aneurysms of any size require repair. (5) Only 5% of ascending aortic aneurysms are due to Marfan's syndrome. There is evidence that around 21% of ascending aortic aneurysms are familial (autosomal dominant); however, this is likely an underestimation. Genetic testing, however, remains a laboratory tool. (6) Probands with ascending aortic aneurysms are more likely to have family members with ascending aortic aneurysms, whereas if the aneurysm is in the descending thoracic aorta, family members will most likely have abdominal aortic aneurysms. (7) Aortic disease above the ligamentum arteriosus is non-arteriosclerotic, whereas below the ligament, it is arteriosclerotic; in fact, those patients with ascending aortic aneurysms are often protected against atherosclerosis. (8) A positive d-dimer has 99% sensitivity for detecting aortic dissection; thus a negative d-dimer can exclude aortic dissection. (9) Beta-blocker therapy, although controversial, is often used clinically. Angiotensin receptor blockers, doxycycline, a matrix metalloproteinase inhibitor, anti-inflammatory agents, statins, and immunosuppressants show promise.
Reviewer's Comments: This excellent review reminds us that ascending and descending aortic aneurysms are 2 distinct disease processes, and a majority of ascending aortic aneurysms may be familial. Aortic aneurysm is life threatening but indolent disease, and rapid changes in size do not occur in the absence of dissection. A clinical pearl is that a negative d-dimer makes aortic dissection unlikely. Newer biomarkers, genetic screening methods, imaging modalities, and stent therapies are being developed. (Reviewer-Anoop C. Parameswaran, MD).

Keywords: Thoracic Aortic Aneurysm, Genetic

Print Tag: Refer to original journal article

Warranty Period of Coronary Artery Calcium

Determinants of Coronary Calcium Conversion Among Patients With a Normal Coronary Calcium Scan: What Is the "Warranty Period" for Remaining Normal?

Min JK, Lin FY, et al:

J Am Coll Cardiol 2010; 55 (March 16): 1110-1117

If a patient's coronary artery calcium score is 0, the risk of converting to a positive calcium score is low in the first 4 years.

Background: The natural progression of coronary artery calcification (CAC) is not well known.
Objective: To assess the conversion rate of CAC and to evaluate factors predicting progression of CAC.
Participants/Methods: 422 patients referred for CAC screening on a clinical basis who had a 0 CAC score were studied with yearly CAC scans. In addition, 621 patients with a CAC score of >0 were also studied as a contrast group.
Results: 92.2% of patients with an initial CAC score of 0 had at least >1 coronary artery disease (CAD) risk factor and a Framingham risk score of 9.3%. Of patients, 25.1% converted to a CAC score >0 during 5 years of follow-up (average CAC score, 19 ± 19). The rate of conversion was fairly linear in the first 2 years and accelerated in years 4 and 5. In a multivariate analysis, diabetes, age >40 years, and smoking independently increased the risk of conversion. However, no single risk factor was associated with accelerated progression. In those with an initial CAC score >0, only baseline CAC independently increased the hazard of progression, and those with higher CAC scores had higher rates of progression. There were 266 patients with a CAC score of 0 and a CAC score of >0 who were propensity matched, and baseline CAC remained the most powerful predictor of progression followed by diabetes and smoking.
Conclusions: In patients with a CAC score of 0, the rate of progression in the first 4 years is non-linear and occurs infrequently. In those with a CAC score of >0, baseline CAC is the strongest predictor of progression.
Reviewer's Comments: This study demonstrates that, in individuals with low-intermediate cardiac risk and a CAC score of 0, the risk of progression to a positive CAC scan is low in the first 4 years. No clinical factors predicted accelerated progression. Thus, in this group of patients, repeat scanning earlier than 4 years is not indicated. Once CAC has developed, baseline CAC score--not traditional risk factors--predict future progression. (Reviewer-Anoop C. Parameswaran, MD).

Keywords: Coronary Calcium, Cardiac CT, Coronary Artery Disease

Print Tag: Refer to original journal article

Stop Coumadin in Afib Patients!

The Risk of Thromboembolism and Need for Oral Anticoagulation After Successful Atrial Fibrillation Ablation.

Themistoclakis S, Corrado A, et al:

J Am Coll Cardiol 2010; 55 (February 23): 735-743

Anticoagulation can be safely stopped in patients undergoing successful atrial fibrillation ablation.

Background: The risk of thromboembolism, typically stroke (cerebrovascular accident [CVA]), is well documented with atrial fibrillation (Afib). Catheter ablation (radiofrequency ablation [RFA]) has emerged as an effective therapy for Afib, but physicians often struggle with the safety of discontinuing anticoagulation (AC) following RFA.
Objective: To evaluate the safety of discontinuation of AC following Afib RFA.
Participants: Consecutive patients at 5 centers who underwent Afib RFA between 2001 and 2005 were included. Patients with prosthetic valves were excluded.
Methods: All patients underwent RFA using pulmonary vein isolation and additional ablation as per instructions from the treating physician. All patients received AC with Coumadin for 3 to 6 months post-RFA. AC was subsequently discontinued regardless of CHADS2 score if patients did not have any recurrence of Afib or atrial tachycardia/atrial flutter over 1 minute in duration, severe pulmonary vein stenosis, or severe left atrial (LA) dysfunction by echocardiogram. Aspirin was maintained following discontinuation of AC. The end points of the study were embolic or hemorrhagic stroke or other bleeding.
Results: AC was discontinued in 2692 patients a median of 4 months after Afib RFA. These patients remained off AC for a median of 25 months. CHADS2 score was 0 in 60%, 1 in 27%, and ≥2 in 13%. AC was continued in 663 patients for a median of 19 months because of arrhythmic recurrence (72%), LA dysfunction (10%), severe pulmonary vein stenosis (3%), or patient/physician preference/other in 15%. The off-AC group was more likely to be male, younger, and have had longer durations of paroxysmal Afib prior to RFA, smaller LA diameters, and lower CHADS2 scores. Two patients off AC (0.07%) experienced ischemic stroke during follow-up. One patient had a CHADS2 score of 0, and the other patient had a CHADS2 score of 1. No arrhythmias were observed in either patient up to the point, and both events apparently occurred in sinus rhythm. The incidence of ischemic stroke was 0.45% in the on-AC group. Major hemorrhage occurred in 1 patient (retroperitoneal bleed; 0.04%) in the off-AC group and in 2% in the on-AC group (2 intracranial hemorrhages, 11 gastrointestinal bleedings).
Conclusions: AC can be safely discontinued in patients post-Afib RFA if they have no known recurrence, LA dysfunction, or pulmonary vein stenosis.
Reviewer's Comments: This is the largest study evaluating AC post-Afib RFA, and it suggests that discontinuation of AC may be an achievable goal for patients afflicted with Afib who undergo RFA. Important highlights from the study include the maintenance of sinus rhythm without arrhythmic recurrence documented through repeated monitoring, maintenance of the majority of patients on aspirin, and ablation performed at very experienced centers. This study was observational and retrospective, and therefore, results are limited. It is unclear if these results persist beyond the reported follow-up period as some late recurrence of Afib has been reported. (Reviewer-Sumeet K. Mainigi, MD).

Keywords: Atrial Fibrillation, Warfarin, Anticoagulation, Stroke, Ablation

Print Tag: Refer to original journal article

OSA, Not Obesity, Accounts for Inflammation in Obese Patients

Vascular Inflammation in Obesity and Sleep Apnea.

Jelic S, Lederer DJ, et al:

Circulation 2010; 121 (March 2): 1014-1021

Obstructive sleep apnea, and the resultant hypoxia, probably account for the inflammation and vascular dysfunction commonly observed in obese patients.

Background: Obstructive sleep apnea (OSA) is highly prevalent in obesity but is often undiagnosed. Obesity and OSA have been associated with vascular inflammation. Unrecognized OSA may be the cause of alterations in vascular function previously attributed to obesity.
Objective: To assess endothelial function in normal weight and obese subjects evaluated for OSA.
Participants: 71 subjects were studied; 38 had OSA (apnea-hypopnea index [AHI] ≥5), while 33 did not. All had a normal physical exam and normal laboratory studies; those with chronic diseases were excluded, and none were on medications.
Methods: Endothelial cells were harvested and assessed for expression of (1) endothelial nitric oxide (eNOS) and phosphorylated eNOS (markers of nitric oxide [NO] production and activity), (2) nitrotyrosine (marker of oxidative stress), and (3) nuclear factor-kappaB (marker of inflammation). Brachial artery flow-mediated dilation (FMD) was measured as an indirect marker of endothelial reactivity. Nineteen patients compliant with continuous positive airway pressure (CPAP; ≥4 hours/night) were restudied 4 weeks later.
Results: Markers of NO production/activity were significantly lower, and markers of inflammation were significantly higher in patients with OSA versus those without; this was true regardless of obesity. When endothelial markers were measured against body mass index, waist circumference, and waist-hip ratio as continuous variables, there were no significant correlations. There were also no significant correlations between obesity and FMD. AHI correlated inversely with markers of endothelial function and directly with markers of inflammation. In OSA patients compliant with CPAP, endothelial function improved, and inflammatory markers decreased on treatment.
Conclusions: OSA rather than obesity is the major determinant of endothelial dysfunction and oxidative stress in obese patients. Without OSA, obesity (by various measures) was not associated with decreased endothelial function, inflammation, or increased oxidative stress. Furthermore, obesity did not increase the effects of OSA on vascular endothelium.
Reviewer's Comments: One of the key limitations in observational research is our inability to account for all potential confounders. This study demonstrates that our previous conception of obesity as a pro-inflammatory state is mistaken. Rather, it's the presence of OSA that promotes inflammation and adversely impacts vascular function. While adipose tissue is a well-known source of inflammatory molecules, it may be that hypoxia is a necessary trigger for initiation of inflammatory cascades. (Reviewer-Gregg S. Pressman, MD).

Keywords: Obesity, Sleep Apnea, Inflammation, Vascular Function

Print Tag: Refer to original journal article

EECP Stops Atherosclerosis Progression

Enhanced External Counterpulsation Attenuates Atherosclerosis Progression Through Modulation of Proinflammatory Signal Pathway.

Zhang Y, He X, et al:

Arterioscler Thromb Vasc Biol 2010; 30 (April): 773-780

The mechanical shear stress produced by enhanced external counterpulsation slows atherosclerosis by downregulating proinflammatory vascular gene expression.

Background: Endothelial cells exposed to high shear stress are protected from atherosclerotic plaque formation. Enhanced external counterpulsation (EECP), a noninvasive treatment for ischemic cardiovascular disease, increases shear stress along endothelial cells. The exact molecular mechanisms underlying clinical benefits remain unclear.
Objective: To examine the effects of EECP on vascular inflammation and atherosclerosis.
Design: Randomized controlled trial.
Methods: 35 domestic male pigs were randomized to a normal diet (NORM, n=7) or a high-cholesterol diet (n=28) for 15 weeks. At 8 weeks, when hypercholesterolemia was achieved, 17 pigs received 34 ± 2 hours of EECP over 7 weeks (EECP group) while on the atherogenic diet. The remaining 11 pigs served as hypercholesterolemic controls (CHOL group). Doppler ultrasound flow examinations and arterial wall shear stress calculations were performed. Serial blood lipid profiles were measured. Atherosclerotic lesions were studied by morphological analysis, quantitative real-time polymerase chain reaction, immunohistochemistry, immunofluorescence, and Western blot analysis.
Results: EECP increased mean shear wall stress by 34% (P =0.019) and decreased pulsatility index (PI) by 17% (P =0.045) compared to baseline. The high-cholesterol diet led to comparable hypercholesterolemia in both CHOL and CHOL+EECP groups as compared to the NORM group (P <0.001). Atherosclerotic lesions developed in both hypercholesterolemic groups; however, the CHOL+EECP group had smaller lesions compared to the CHOL group (P <0.001), associated with a 54% decrease in macrophage accumulation, demonstrating the atheroprotective effect of EECP. EECP also presented a 54% reduction of smooth muscle cell (P <0.01) and 30% reduction of collagen (P =0.01) versus CHOL suggesting EECP changes lesion composition. EECP+CHOL had reduced expression of pro-inflammatory genes as compared to CHOL, namely mitogen-activated protein kinase (MAPK)-p38/nuclear factor (NF)-κB/vascular cell adhesion molecule-1 (VCAM-1) signaling pathway. EECP+CHOL also demonstrates significant decrease in complement activation and C-reactive protein production as compared to CHOL group.
Conclusions: The increased shear stress induced by EECP results in down regulation of proinflammatory gene expression leading to a slowing of atherosclerosis seen in hypercholesterolemia.
Reviewer's Comments: EECP increases shear stress on the endothelium, decreases macrophage accumulation and complement activation, attenuates vascular C-reaction protein expression, and eventually improves vascular inflammation. Pulsatile shear stress curbs monocyte adhesion to endothelium exposed to oxidized lipids and upregulates endothelial nitric oxide synthase to produce nitric oxide. Physical exercise and control of hypertension produce this hemodynamic effect, but few other therapies do aside from EECP. These data provide evidence that limiting mitogen-activated protein kinase-p38 and nuclear factor-kappaB activation in plaques could represent a molecular mechanism by which EECP modulates inflammatory responses to hypercholesterolemia, contributing to the observed clinical benefits of EECP. (Reviewer-Debra L. Braverman, MD).

Keywords: Atherosclerosis, Enhanced External Counterpulsation, Endothelial Shear Stress

Print Tag: Refer to original journal article

Strict Heart Rate Control May Be of Little Value for Afib Tx

Lenient Versus Strict Rate Control in Patients With Atrial Fibrillation.

Van Gelder IC, Groenveld HF, et al:

N Engl J Med 2010; March 15 (): epub ahead of print

A strategy of strict heart rate control in permanent atrial fibrillation may not be as valuable as practice guidelines may suggest.

Background: In some patients with atrial fibrillation (Afib), treatment is directed at heart rate (HR) rather than rhythm control. Guidelines recommend strict HR control when such a strategy is pursued. These guidelines are not evidence-based, and the optimal HR goal is unknown.
Objective: To compare outcomes associated with strategies of strict versus more lenient HR control in patients with permanent Afib.
Design: Prospective, multicenter randomized study testing the hypothesis that a more lenient HR control strategy is non-inferior to a strategy of strict rate control.
Participants/Methods: All patients had permanent Afib for a minimum of 12 months, were aged ≤80 years, and had a resting HR of >80 bpm at enrollment. HR targets were achieved with calcium-channel blockers, beta-blockers, or digoxin alone or in combination. The strict HR group had a target HR of <80 bpm at rest and <110 bpm with moderate exercise. In comparison, the target resting HR was <110 bpm for the lenient HR group. Maximum follow-up was 3 years. The primary outcome was the composite of cardiovascular death, heart failure hospitalization, stroke, major bleeding, life-threatening drug side effects, arrhythmic events, and need for device implantation. A total of 311 patients were included in the lenient HR group and 303 in the strict HR group. Groups were well matched in baseline demographic characteristics and time with therapeutic international normalized ratio.
Results: At the end of the dose-adjustment period, the resting HR in the lenient HR group was 93 ± 9 bpm versus 76 ± 12 bpm for the strict HR group (P <0.001). During longer follow-up, the mean HR in the lenient HR group was 85 bpm versus 75 bpm in the strict HR group. Target HR was more difficult to achieve in the strict HR group, and up to 25% of patients never achieved target HR. The primary outcome occurred in 81 patients (38 in the lenient HR group and 43 in the strict HR group). The 3-year estimated incidence of the primary outcome was 13% in the lenient HR group and 15% in the strict HR group (P =ns). The results demonstrated that the lenient-control strategy was non-inferior to the strict-control strategy. Similar results were noted for individual components of the composite outcome. Subgroups with CHADS2 scores ≥2 and those <2 had similar findings.
Conclusions: In patients with permanent Afib, a strategy of lenient HR control is non-inferior to a strategy of strict HR control in regard to a composite of cardiovascular morbidity and mortality outcomes.
Reviewer's Comments: This is a case of data and science not agreeing with what is considered standard practice and common sense. I believe more extensive data are needed to validate the findings of this study. (Reviewer-Khalid Almuti, MD).

Keywords: Permanent Atrial Fibrillation, Rate Control

Print Tag: Refer to original journal article

Acute MI, Diabetes, Drug-Eluting Stent -- Triple Threat or Tantalizing Trio?

Outcomes in Diabetic Versus Nondiabetic Patients Who Present With Acute Myocardial Infarction and Are Treated With Drug-Eluting Stents.

Syed AI, Ben-Dor I, et al:

Am J Cardiol 2010; 105 (March 15): 819-825

In diabetic patients with an acute myocardial infarction, drug-eluting stents may be most suitable.

Background: Diabetes mellitus (DM) has been shown to predict an adverse outcome in patients with coronary artery disease. Patients with DM have a greater risk of mortality and cardiovascular events after percutaneous coronary intervention (PCI) than do those without DM. Data on using bare-metal stents versus drug-eluting stents (DESs) in diabetic patients with an acute myocardial infarction (MI) is also not clear.
Objective: To evaluate whether use of DESs could reduce 1-year major adverse cardiac event (MACE) rates in patients with DM compared to those without.
Participants/Methods: 161 patients with DM and 395 without DM underwent primary PCI for acute MI and were treated with DESs. All patients with cardiac arrest or cardiogenic shock were excluded. The 1-year MACE rates, defined as death, Q-wave MI, or target lesion revascularization, were compared between groups.
Results: Patients with DM were sicker on initial presentation. One-year MACE rates were significantly increased in those with DM compared to those without DM. All-cause mortality was the main event, mainly due to out-of-hospital death. There were no significant differences in Q-wave MI, target lesion revascularization, stent thrombosis, type of DES used, or procedure-related renal failure between groups. After adjusting for age, gender, race, systemic hypertension, peripheral artery disease, and history of chronic renal failure between groups, there was no statistical difference in 1-year death or MACE rates.
Conclusions: Following correction for comorbid conditions, there were no differences seen in 1-year MACE or death rates in patients with or without DM who presented with acute MI and had interventions with DESs.
Reviewer's Comments: Among patients with DM and stable coronary artery disease, use of DESs reduces the risk of subsequent MACE as compared to bare-metal stents. However, beneficial effects of intervening with DESs in patients with DM and an acute coronary syndrome is not clear. Also controversial is using DESs versus bare-metal stents in patients with an acute MI, with too few patients allowing for adequate subset analysis in those patients with DM. This paper is therefore important in showing that, after adjusting for differences in baseline characteristics, there was no statistical difference in MACEs at 1-year between those patients with and without DM. DM is, by its very nature, a chronic illness, which may result in complications developing slowly and may therefore be less predictive of an outcome after an acute event. There has been concern about using DESs in the setting of an acute MI due to delayed healing and an increased incidence of late stent thrombosis, but there was no such increase in this study's DM population. (Reviewer-Suraj Maraj, MD).

Keywords: Drug-Eluting Stent, Acute Myocardial Infarction, Diabetic Patients

Print Tag: Refer to original journal article

In Multivessel Disease, FFR Picks Up Ischemic Territories Missed by MPI

Fractional Flow Reserve and Myocardial Perfusion Imaging in Patients With Angiographic Multivessel Coronary Artery Disease.

Melikian N, De Bondt P, et al:

J Am Coll Cardiol Intv 2010; 3 (March): 307-314

Fractional flow reserve is more sensitive than myocardial perfusion imaging in detecting ischemic territories in patients with multivessel disease.

Background: Myocardial perfusion imaging (MPI) during stress testing detects ischemic territory based on a relative comparison to normally perfused regions. Detection of ischemia requires at least 1 non-stenotic coronary artery so that normally perfused territory is available for qualitative comparison. MPI, therefore, might be less accurate in detecting multivessel coronary artery disease due to "balanced ischemia." Also, in the setting of multivessel stenoses, MPI might not be accurate in determining the relative severity of each stenosis. Fractional flow reserve (FFR) measurement is a well-studied, invasive alternative to MPI by which the physiologic significance of an individual coronary stenosis can be assessed. FFR is determined by passing a pressure wire across a stenosis and measuring the ratio of pressures distal to and proximal to the stenosis after achievement of steady-state hyperemia with adenosine infusion. The FFR for any given stenosis is independent of stenoses in other vessels. Multivessel FFR measurement is potentially more accurate in determining the significance of individual coronary stenoses than MPI.
Objective: To compare the ability of MPI versus FFR to detect ischemia in multivessel disease.
Design: Prospective study.
Participants/Methods: 67 stable patients with 2- to 3-vessel disease appropriate for PCI angiographically underwent MPI followed by FFR-guided PCI (PCI when FFR <0.8). Patients with unstable syndromes or abnormal left ventricular wall motion were excluded. Ischemic myocardial territories as detected by MPI and by FFR were compared.
Results: MPI and FFR detected identical ischemic territories in 28 patients (42%). MPI underestimated the number of ischemic territories compared to FFR in 24 patients (36%). In patients with multi-territory ischemia, MPI generally detected the territory with the lowest FFR. In general, the concordance between MPI and FFR was low, except in the case of patients with only 1 ischemic territory by FFR.
Conclusions: Multivessel FFR assessment should be considered when important decisions regarding revascularization are being made.
Reviewer's Comments: This unique study looked at stable patients with multivessel disease to compare ischemia detection by MPI versus FFR. FFR, a validated and reproducible index, was found to be more sensitive in detecting ischemic territories in this population compared to MPI. In addition to the lack of randomization and clinical follow-up, a limitation of this study is the assumed ischemic FFR for occluded vessels. This was done for 12 occluded vessels of the total 201 vessels. If the collateral supply is adequate, all occluded territories might not necessarily be ischemic nor benefit from revascularization. Based on improved outcomes of patients treated with this approach in the randomized FAME study (now with 2 years of follow-up), I agree with the current authors' conclusions. Longer clinical follow-up will hopefully give us the durability of FFR assessment. (Reviewer-Parul B. Patel, MD).

Keywords: Fractional Flow Reserve, Multivessel Coronary Artery Disease, Myocardial Perfusion Imaging

Print Tag: Refer to original journal article

Lower Is Not Necessarily Better for BP Control in Diabetes Mellitus

Effects of Intensive Blood-Pressure Control in Type 2 Diabetes Mellitus.

The ACCORD Study Group:

N Engl J Med 2010; March 14 (): epub ahead of print

Systolic blood pressure control to <140 mm Hg is probably sufficient to reduce cardiovascular outcomes in patients with diabetes.

Background: The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7) recommends systolic blood pressure (BP) control to <130 mm Hg in patients with diabetes. There are very little randomized data supporting this strategy.
Objective: The Action to Control Cardiovascular Risk in Diabetes (ACCORD) blood pressure trial (ACCORD BP) was designed to test whether intensive BP control with a target systolic BP ≤120 mm Hg would effectively decrease cardiovascular outcomes as compared to standard BP control with a target systolic blood pressure ≤140 mm Hg.
Participants: Patients with diabetes mellitus and hemoglobin A1c of >7.5% and age ≥40 years with coronary artery disease or age ≥55 years with significant risk factors for coronary artery disease were included. Patients with morbid obesity, creatinine >1.5 mg/dL, and other serious illnesses were excluded from the study.
Design: The ACCORD trial randomized 10,251 patients to intensive glycemic therapy versus standard therapy for the ACCORD glycemia trial. Half of these patients (n=4733) were randomized in a 2 x 2 factorial design to the ACCORD BP trial--intensive therapy group (n=2362) and the standard group (n=2371). Currently available and approved treatment strategies were used for BP control in both arms. Major cardiovascular event, which was a composite of nonfatal myocardial infarction, nonfatal stroke, and cardiovascular death, was the primary outcome. There were multiple prespecified secondary end points including death from any cause.
Results: At baseline, the patients were evenly matched in both groups. The mean age of the patients was approximately 62 years with 48% females. Approximately one third had cardiovascular disease at baseline. The patients were followed for a mean duration of 4.7 years. At the end of 1 year of follow-up, the mean BP in the intensive therapy group was 119 mm Hg and 134 mm Hg in the standard group. The difference persisted during follow-up. As expected, the intensive therapy group on average used more antihypertensive medications (3.4) versus the standard therapy group (2.1). There were significantly more adverse events related to antihypertensive medications in the intensive therapy group as compared to the standard therapy group. There was no significant difference in the composite primary end point or the prespecified secondary end points except for a nominal decrease in stroke rate in the intensive therapy group (0.32% vs 0.53 %/year).
Conclusions: In this large multicenter trial, intensive BP control did not decrease cardiovascular events as compared to standard therapy.
Reviewer's Comments: This study also shows that intensive therapy may be potentially harmful and is of little benefit as compared to lowering blood pressure to the mid 130s. (Reviewer-Pradeep S. Arumugham, MD).

Keywords: Blood Pressure Target, Diabetes Mellitus

Print Tag: Refer to original journal article

Do Too Many Asymptomatic Patients Go to Cardiac Catheterization?

Low Diagnostic Yield of Elective Coronary Angiography.

Patel MR, Peterson ED, et al:

New Engl J Med 2010; 362 (March 11): 886-895

Noninvasive testing adds little to clinical risk assessment in low-risk populations.

Background: Current guidelines attempt to limit the number of referrals for coronary angiography that ultimately prove not to have significant obstruction. Toward this end, clinical risk assessment is recommended, with observation only for those at lowest risk, and noninvasive testing when risk is intermediate.
Objective: To evaluate the effectiveness of such a strategy. The impetus behind it is the rapidly growing cost of imaging services.
Methods: The CathPCI Registry of the National Cardiovascular Data Registry was used; this is a voluntary registry of clinical data provided by sites across the U.S. Patients with urgent/emergent procedures or known coronary artery disease (CAD) were excluded. Demographic information, clinical risk factors, and results of noninvasive tests (ECG, exercise/pharmacologic stress tests, radionuclide/CT/other heart scans) were collected.
Results: 1,989,779 patients underwent catheterization at 663 sites; after exclusions, 397,954 (20%) were entered into the study. Obstructive CAD (≥50% left main or ≥70% for other vessels) was found in 38% (41% had ≥50% in any vessel). In total, 39% had no CAD (<20% stenosis in all vessels). Patients with CAD were older, more likely male, had more diabetes/hypertension/hyperlipidemia, and were more likely to have angina (P <0.001 for all). Noninvasive testing was performed in 84%, with a positive result in 69%. Noninvasive testing was not performed prior to catheterization in 17% of low-risk (modified Framingham score) patients, 16% with intermediate risk, and 15% with high risk. A positive noninvasive test was an independent predictor of CAD (OR, 1.28), but less so than clinical risk factors. Adding noninvasive testing to a risk model that included Framingham score, other clinical factors (body mass index, peripheral/cerebral vascular disease, chronic obstructive pulmonary disease, need for dialysis), and angina had a limited effect on prediction (C-statistic increased from 0.761 to 0.764).
Conclusions: Among patients without known CAD, coronary angiography had a low diagnostic yield. Noninvasive testing was frequently used in high-risk patients but not always performed in low/intermediate-risk patients. Overall, 30% of patients were asymptomatic, whereas invasive treatment was primarily beneficial in symptomatic patients. Improvements in clinical risk assessment and quality of noninvasive treatment are needed.
Reviewer's Comments: This study highlights several troubling aspects of current assessment of chest pain patients. Because of perceived accuracy and the desire for "high tech," objective evaluation, use of noninvasive tests has rapidly increased. Yet these tests have significant limitations, most especially a high false-positive rate in low-risk populations. This can lead to further testing with associated increases in cost and patient anxiety. Nuclear stress testing is also problematic because of the high radiation exposure it entails. Not only do we need better noninvasive testing, we need to be more judicious in its application. There is still no substitute for experience and good clinical judgment. (Reviewer-Gregg S. Pressman, MD).

Keywords: Coronary Angiography, Noninvasive Testing, Clinical Risk

Print Tag: Refer to original journal article

Is Surface ECG Better Than Echo for Predicting CRT Response?

Analysis of Ventricular Activation Using Surface Electrocardiography to Predict Left Ventricular Reverse Volumetric Remodeling During Cardiac Resynchronization Therapy.

Sweeney MO, van Bommel RJ, et al:

Circulation 2010; 121 (February 9): 626-634

Left ventricular activation time can be gleaned from surface ECG when QRS notching is present.

Background: Up to one third of systolic heart failure patients who receive cardiac resynchronization therapy (CRT) are nonresponders. The reasons are not completely understood but probably relate to interactions between cardiac substrate and pacing-related changes in ventricular activation.
Objective: To hypothesize that response to CRT can be predicted by baseline and post-CRT ECG variables.
Participants/Methods: 202 consecutive patients with NYHA class III to IV heart failure, ejection fraction (EF) ≤35%, and left bundle branch block (LBBB) were studied. The primary end point was left ventricular (LV) reverse remodeling at 6 months, defined as ≥10% reduction in end-systolic volume (ESV) by echocardiography (biplane Simpson method). Various ECG analyses were performed including measurement of LV activation time (LVAT) defined from notching of the QRS (transition point from RV to LV activation) to its end. When no notching was present, LVAT was estimated using a linear regression formula. Analyses also included estimation of LV scar by Selvester QRS score.
Results: Larger LVAT was associated with a greater probability of remodeling up to a plateau of 125 ms (OR, 1.30; 95% CI, 1.11 to 1.52). QRS score was also predictive of response: 78% for lowest quartile (0 to 3) versus 45% for highest quartile (>9). Post-pacing variables were also useful: increasing R amplitude in V1 to V2 (≥4.5 x baseline) and a shift from left axis deviation to right axis deviation predicted a positive CRT response (OR, 2.76 [95% CI, 1.01 to 7.51] and OR, 2.00 [95% CI, 0.99 to 4.02], respectively).
Conclusions: The probability of reverse remodeling by use of CRT in systolic heart failure with LBBB can be predicted by ECG characterization of ventricular activation before and after pacing. The mechanism appears to involve electrical wavefront fusion. Increasing LVAT at baseline positively influences this process while increasing scar volume negatively influences it. Evidence of fusion on the paced ECG increases the chances of a positive response, though exceptions still exist.
Reviewer's Comments: Proper identification of candidates for CRT remains a challenge. Despite great efforts to devise objective echocardiographic measures to predict a positive response, none of the proposed methods have proved reliable. The authors of the current paper have been heavily involved in this research. They now propose looking at the baseline and paced ECG in greater detail. Their method, if validated in larger prospective studies, would be extremely useful as it could be readily incorporated into ECG software. However, the accompanying editorial by Ellenbogen notes that the current 60% to 70% response rate (using simple QRS duration >120 ms) compares favorably with other treatment modalities, and that it's possible no method will be found that exceeds this. (Reviewer-Gregg S. Pressman, MD).

Keywords: Cardiac Resynchronization Therapy, Left Bundle Branch Block, ECG

Print Tag: Refer to original journal article

Dopamine, Norepinephrine for Shock -- Not Quite Equal

Comparison of Dopamine and Norepinephrine in the Treatment of Shock.

De Backer D, Biston P, et al:

N Engl J Med 2010; 362 (March 4): 779-789

When used for treatment of shock, dopamine leads to higher heart rates than does norepinephrine.

Background: Shock of any cause is associated with high mortality. Dopamine and norepinephrine are frequently used agents when volume resuscitation fails to restore blood pressure (BP). However, they have differing effects on renal and splanchnic beds and there are observational data suggesting that dopamine may be associated with higher mortality.
Objective: To evaluate whether the choice of norepinephrine over dopamine as the first-line vasopressor agent can reduce the rate of death among patients in shock.
Methods: Entry criteria included mean BP <70 (or systolic BP <100) after adequate fluid resuscitation, and signs of tissue hypoperfusion. Primary outcome was death at 28 days. Secondary outcomes included survival at 6 and 12 months. Adverse events, particularly arrhythmias, were also monitored. The study was conducted in a double-blind manner with results analyzed on an intention-to-treat basis.
Results: 1679 patients from 8 European centers were enrolled. Septic shock was seen in 62%, cardiogenic shock in 17%, and hypovolemic shock in 16%. Heart rate increases were greater in the dopamine group but changes in cardiac index, central venous pressure, oxygen saturation, lactate levels, and total urine output were similar. There were no significant differences in death at 28 days, 6 months, or 12 months. However, arrhythmia was more common in the dopamine group (24% vs 12%; P <0.001), with atrial fibrillation comprising 86% of all arrhythmias. In addition, predefined subgroup analysis showed higher 28-day mortality in those with cardiogenic shock receiving dopamine (P =0.03)
Conclusions: This study observed a high mortality in patients with diverse causes of shock, close to 50% at 28 days. Overall, there was no significant difference between dopamine and norepinephrine. However, dopamine was associated with significantly higher rates of arrhythmia and a higher death rate in the subgroup with cardiogenic shock. Current ACC/AHA guidelines recommending dopamine as first-line therapy for hypotension in the setting of acute myocardial infarction should be reconsidered.
Reviewer's Comments: Studies in critically ill patients are difficult to accomplish and therefore fairly rare. Much of what we do in the ICU is based on traditional teaching as opposed to evidence-based treatment. Norepinephrine has been viewed as potentially more dangerous than dopamine, to be used more as a last resort than first-line agent for hypotension, at least among medical ICU patients. This study challenges that concept and further points out the potential arrhythmic risk of dopamine. In addition, dopamine appears to be detrimental in cardiogenic shock, possibly because of associated higher heart rates and higher oxygen demand. The accompanying editorial also points out that dopamine is the precursor for norepinephrine and acts indirectly. Some of its effects appear due to neuronal release of epinephrine and norepinephrine; thus it may be less effective when stores of these agents are reduced, such as in chronic heart failure. (Reviewer-Gregg S. Pressman, MD).

Keywords: Dopamine, Norepinephrine, Shock, All-Cause Mortality, Arrhythmia

Print Tag: Refer to original journal article

Olmesartan Causes Plaque Regression

Impact of Olmesartan on Progression of Coronary Atherosclerosis: A Serial Volumetric Intravascular Ultrasound Analysis From the OLIVUS (Impact of Olmesartan on Progression of Coronary Atherosclerosis: Evaluation by Intravascular Ultrasound) Trial.

Hirohata A, Yamamoto K, et al:

J Am Coll Cardiol 2010; 55 (March 9): 976-982

This study suggests a positive role in a potentially lower rate of coronary atheroma progression through administration of olmesartan, an angiotensin receptor-blocking agent, for patients with stable angina pectoris.

Background: Chronic activation of the renin-angiotensin system is a contributor to atherosclerosis.
Objective: To assess the effect of olmesartan (angiotensin receptor blocker) on the progression of coronary atherosclerosis assessed by intravascular ultrasound (IVUS).
Participants/Methods: 247 patients with stable angina pectoris and hypertension scheduled for percutaneous coronary intervention were randomized to control (121 patients) or olmesartan (126 patients). Twelve to 16 months later, IVUS of the original artery was performed. The primary outcome assessed was change in plaque volume by IVUS. Major cardiovascular adverse events were also assessed.
Results: 102 patients in the IVUS arm and 103 patients in the olmesartan arm completed the study. Baseline characteristics were similar between both arms. On follow-up, there were no differences in major cardiovascular events. The total atheroma volume increased by 5.4% in the control arm and was minimally changed in the olmesartan arm (0.6%). The percent atheroma volume also increased by 3.1% in the control arm compared to –0.7% in the olmesartan arm. Multiple regression analysis revealed that olmesartan was one of the variables that decreased atheroma progression.
Conclusions: Olmesartan is effective in slowing the progression of coronary atherosclerosis in patients with stable angina.
Reviewer's Comments: Prior IVUS studies have shown slowing and even regression of atherosclerosis with drugs such as statins and pioglitazone. This trial showed that olmesartan, on a background of good medical therapy, including statins, was able to cause plaque regression. There was, however, no significant effect on cardiovascular events, likely due to the small number of patients and short follow-up. (Reviewer-Anoop C. Parameswaran, MD).

Keywords: Olmesartan, Plaque, Intravascular Ultrasound

Print Tag: Refer to original journal article

An Exclusively Female CR Program Enhances Attendance

Predicting Cardiac Rehabilitation Attendance in a Gender-Tailored Randomized Clinical Trial.

Beckie TM, Beckstead JW:

J Cardiopulm Rehabil Prev 2010; March 4 (): epub ahead of print

A gender-tailored cardiac rehabilitation program allows for increased attendance by women and helps to identify baseline risk factors for dropping out of the program.

Background: Coronary artery disease (CAD) is the leading cause of death in women. Cardiac rehabilitation (CR) reduces morbidity and mortality in CAD but is underutilized by women, and those who do participate exhibit poor attendance. Gender-specific programs may be uniquely effective in meeting women's distinctive needs.
Objective: To determine whether CR attendance by women is influenced by a motivationally enhanced, gender-tailored CR program compared to traditional CR, and to determine which baseline characteristics predict attendance.
Design: Single-blind, randomized controlled trial.
Participants: 252 women with CAD (mean age, 63 years) diagnosed with an anterior myocardial infarction, angina, or having undergone coronary artery bypass graft surgery or percutaneous coronary intervention within the last year, who were referred to outpatient CR were randomized to one of two 12-week programs: traditional CR (TCR; n=111) or a gender-tailored, behavioral enhancement group (GTCR; n=141).
Methods: Investigators collected baseline data and participants underwent an exercise tolerance test and were then randomized to 1 of 2 groups. The TCR group did aerobic exercise and resistance training 3 times per week and 8 education classes focusing on CAD risk factor modification. GTCR was identical to TCR except participants exercised exclusively with women and they had 10 education classes that focused on motivation counseling to assess readiness to change behaviors (eating, exercise, stress). Patients were assessed for perceived health status, quality of life, anxiety, depression, social support, level of hope, body mass index, exercise capacity, smoking status, and marital status.
Results: Both groups were the same in all measured variables at baseline. TCR attended fewer exercise and education sessions than GTCR (77% vs 90% and 56% vs 87%, respectively). Group assignment accounted for 5% of the variance in exercise attendance and 24% of the variance in education attendance (P <0.001). After controlling for group assignment, only anxiety, marital status, and smoking status accounted for 17% of the variance in exercise attendance, and marital status and smoking status were significant baseline predictors of education attendance (P <0.001).
Conclusions: The GTCR program favorably impacted exercise attendance by 13% and education attendance by 31%. Further research studying the value of gender-sensitive, motivationally enhanced cardiac rehabilitation for women compared with traditional programs is necessary.
Reviewer's Comments: Acknowledging the patients' readiness to change behaviors contributed to the greater attendance in the gender-tailored group. Clarifying their rationale for change may help women follow through with healthy behaviors. Social support obtained from women in their cohort helped their psychosocial needs. Improved understanding of baseline characteristics that reliably predict attendance in CR may help target women for specialized interventions to diminish premature discontinuation of the program. (Reviewer-Debra L. Braverman, MD).

Keywords: Coronary Artery Disease, Gender, Predictions

Print Tag: Refer to original journal article

The Burden of Afib in Patients With ICDs

Prognostic Importance of Atrial Fibrillation in Implantable Cardioverter-Defibrillator Patients.

Borleffs CJ, van Rees JB, et al:

J Am Coll Cardiol 2010; 55 (March 2): 879-885

Presence of permanent atrial fibrillation in implantable cardioverter-defibrillator patients portends a poor prognosis.

Background: Many patients are receiving implantable cardioverter-defibrillators (ICD) for primary prevention of sudden cardiac death. The majority of these patients have significant left ventricular (LV) dysfunction. The incidence of atrial fibrillation (Afib) in patients with LV dysfunction is considerable. The morbidity and mortality of Afib in this population is especially high.
Objective: To investigate the prognostic implication of having Afib of any type at ICD implant.
Design/Methods: Baseline data on patients receiving ICDs at a single center were collected prospectively. Patients were grouped into 4 groups: no Afib, paroxysmal Afib, persistent Afib, and permanent Afib. Patients were followed every 3 to 6 months. ICDs were interrogated for appropriate and inappropriate shocks. Follow-up included all-cause mortality.
Results: 913 consecutive patients were included in the analysis with a mean follow-up of 833 days. The group had 79% males and a mean age of 62 years. Mean LV ejection fraction was 32%. Among patients, 663 (63%) had no prior history of Afib. Afib groups included 84 patients (9%) with paroxysmal Afib, 64 (7%) with persistent Afib, and 102 (11%) with permanent Afib. Not surprisingly, patients with any type of Afib were on average older, had more heart failure, and were more often on diuretics, anti-arrhythmic drugs, and anticoagulants compared to non-Afib patients. During follow-up, 117 (13%) patients died. The 3-year cumulative mortality rate for the groups was as follows: no Afib, 12%; paroxysmal Afib, 15%; persistent Afib, 17%; and permanent Afib, 32%. These numbers suggested that mortality for patients with paroxysmal or persistent Afib were statistically similar to patients without Afib. In contrast, patients with permanent Afib had a 70% increase in mortality (hazard ratio [HR], 1.7) compared to no-Afib patients. Appropriate ICD therapy (shock or antitachycardia pacing) occurred in 26% to 29% of patients with no Afib, paroxysmal Afib, or persistent Afib. This is in contrast to 49% of patients with permanent Afib (HR, 2.2). Similar findings were noted for appropriate shocks alone. Patients with any type of Afib had more inappropriate ICD shocks (28% paroxysmal, 18% persistent, and 32% permanent Afib) compared to 13% in the no-Afib group. The HR for inappropriate shocks (compared to the no-Afib group) was 2.7 in those with permanent Afib and 2.9 in those with paroxysmal Afib.
Conclusions: In the general ICD patient population, Afib of any type is quite common. Patients with permanent Afib have nearly double the mortality and risk of appropriate or inappropriate ICD therapy. Patients with paroxysmal and persistent Afib have similar mortality and risk of appropriate device therapy but a higher risk of inappropriate shocks compared to controls.
Reviewer's Comments: Patients with permanent Afib appear to fare worse compared to all others. This probably indicates that this is a sicker group of patients and their Afib is a marker of more advanced heart disease. (Reviewer-Khalid Almuti, MD).

Keywords: Atrial Fibrillation, Implantable Cardioverter-Defibrillators, Incidence, Prognosis

Print Tag: Refer to original journal article

HR Response to Adenosine, Regadenoson Blunted in Hyperglycemic Patients

Blunting of the Heart Rate Response to Adenosine and Regadenoson in Relation to Hyperglycemia and the Metabolic Syndrome.

Hage FG, Perry G, et al:

Am J Cardiol 2010; 105 (March 15): 839-843

Factors that precede development of diabetes mellitus may be associated with cardiac autonomic neuropathy and may explain the contribution of hyperglycemia and metabolic syndrome to cardiovascular risk.

Background: There is an increase in heart rate (HR) during administration of adenosine and regadenoson when performing myocardial perfusion imaging (MPI). This is secondary to direct stimulation of the sympathetic nervous system. Prior data have shown that patients with diabetes mellitus (DM) have a blunted HR response due to cardiac autonomic dysfunction.
Objective: To determine whether HR response to these pharmacological stressors is related to hyperglycemia and the metabolic syndrome (MS).
Methods: Changes in HR were assessed in 2000 patients (643 with DM) in the Adenoscan Versus Regadenoson Comparative Evaluation for Myocardial Perfusion Imaging trials, with a focus on MS status and blood sugar level on the day of MPI. MS was defined as the presence of ≥3 of 5 criteria as per the American Heart Association.
Results: There was a lower HR response in patients with MS (P <0.001). There was also a stepwise decrease in the HR response as the number of MS features increased (–0.92% for every additional MS criterion; P <0.05), irrespective of DM status. MS was also independently related to the HR response on top of DM, renal function, left ventricular function, gender, age, baseline HR, blood pressure, and beta-blocker use. This overall model was significantly associated with the HR response (P <0.001) and explained 30% of its variation. A stepwise decrease in HR response for increasing blood sugar levels was also observed. This blunting of the HR response was present even after controlling for DM and MS (0.60 ± 0.08% per 10 mg/dL; P <0.001).
Conclusions: HR response to adenosine and regadenoson is blunted in patients with hyperglycemia and/or MS. This suggests that factors that precede development of DM may be associated with cardiac autonomic neuropathy and may explain the contribution of hyperglycemia and MS to cardiovascular risk.
Reviewer's Comments: In DM, cardiac autonomic neuropathy is a known complication that is associated with an increased incidence of cardiac events and unfavorable outcomes. This study importantly illustrates that patients with MS and hyperglycemia have a decreased HR response to the A_{2A} agonists adenosine and regadenoson, which is independent of their diabetic status. It is notable that amongst the MS criteria, those most closely linked to insulin resistance (hyperglycemia, obesity, and hypertension) were most significantly predictive of a blunted heart rate response. Those criteria associated with dyslipidemia showed no significant association. It is therefore suggested that these factors of MS that present the highest risk for developing DM may also confer cardiac autonomic neuropathy early in the pre-DM phase. Finally, this study alludes that the combination of 3 parameters (ejection fraction, perfusion, and HR response) in a combined index may provide the optimal prognostic information from a vasodilator stress test. (Reviewer-Suraj Maraj, MD).

Keywords: Blunting, Heart Rate, Myocardial Perfusion Imaging, Cardiac Prognosis

Print Tag: Refer to original journal article

Left Ventricular Non-Compaction--From Diagnosis to Outcomes

Left Ventricular Non-Compaction: Travelling the Road From Diagnosis to Outcomes.

Lewin M:

J Am Soc Echocardiogr 2010; 23 (January): 54-57

Myocardial changes in left ventricular non-compaction are predominantly confined to apical and mid-left ventricular posterior wall segments.

Discussion: This nice editorial discusses left ventricular non-compaction (LVNC). The condition was first described in 1966 when dense trabeculations were seen at cardiac catheterization on left ventriculography. Some other names include immature myocardium, hypertrabeculation of the myocardium, and myocardium spongiosum. LVNC has been included as a separate class of cardiomyopathies by the AHA in the 2006 scientific statement. Population surveys suggest that LVNC may constitute as many as 10% of all cardiomyopathic patients. The traditional Jenni diagnostic criteria for LVNC include (1) absence of coexisting cardiac structural abnormalities that would be expected to result in excessively high ventricular pressure; (2) numerous, excessively prominent trabeculations and deep intertrabecular recesses supplied by intraventricular blood identified using color Doppler echocardiography; (3) myocardial changes predominantly confined to apical and mid-left ventricular posterior wall segments (typically these regions are hypokinetic); and (4) an end-systolic ratio of thick non-compacted layer to thin compacted layer >2. There have been a variety of alternative imaging modalities and echocardiographic tools studied in an attempt to improve diagnostic accuracy. Cardiac MR provides accurate segmental distribution of the disease process similar to that found via assessment of pathological specimens and echocardiographic imaging. Its highest sensitivity, specificity, and predictive value are found when the non-compacted/compacted ratio is >2.3 during diastole (as opposed to 2:1 ratio during systole used for echocardiographic diagnosis). Other modalities include contrast echocardiography and 3-D echocardiographic imaging. LVNC has features that overlap other forms of cardiomyopathy (hypertrophic, dilated, and restrictive). One study found a significant correlation between an abnormal lateral mitral tissue Doppler Ea velocity and development of either primary end points (death or transplantation) or secondary end points (hospitalizations). The approach to a pediatric patient with LVNC typically includes: echocardiographic diagnosis, with careful application of diagnostic criteria; cardiac MRI when needed to clarify diagnosis; evaluation for metabolic, mitochondrial, and genetic etiologies; performance of skeletal muscle biopsy when mitochondrial abnormality is being considered; neurologic exam when appropriate; screening echocardiographic evaluations of first-degree relatives; treatment with multivitamins, afterload reduction, beta-blockers (patients with systolic dysfunction), calcium-channel blockers (hypertrophic form), and antiarrhythmics as needed; anticoagulation for trabecular thrombi and embolic events; follow-up for "undulating phenotype" with transition from hypertrophic to dilated cardiomyopathy; and transplantation referral for intractable symptoms.

Reviewer's Comments: The author further mentions that because LVNC is being increasingly recognized and because diagnostic methods and criteria vary, it is appropriate for those making diagnoses of LVNC to specify the methods and diagnostic findings. (Reviewer-Sahil Mehta, MD).

Keywords: Left Ventricular Non-Compaction, Diagnosis, Imaging

Print Tag: Refer to original journal article

Williams-Beuren Syndrome--A Multisystem Genetic Disorder

Williams–Beuren Syndrome.

Pober BR:

New Engl J Med 2010; 362 (January 21): 239-252

Supravalvular aortic stenosis, at the level of the sinotubular junction, is commonly seen in the Williams–Beuren syndrome.

Discussion: Williams–Beuren (WB) syndrome is a complex medical and neurodevelopmental disorder with characteristic constellation of symptoms. There also exists considerable phenotypic variability. The syndrome involves a microdeletion of chromosome 7. The deletion arises on either the maternally or the paternally inherited chromosome 7 and is sporadic. Fluorescence in situ hybridization (FISH) establishes the diagnosis of WB syndrome by showing the presence of a single ELN (elastin gene) allele only rather than 2 alleles. Characteristic facies in this syndrome include flat nasal bridge, short upturned nose, periorbital puffiness, and a delicate chin in children. Cardiac, endocrine and nervous system abnormalities most affect morbidity and mortality in this syndrome. Cardiovascular manifestations of the WB syndrome include stenosis of medium and large arteries from thickening of vascular media from smooth muscle overgrowth. The stenosis is most commonly at the sinotubular junction (supravalvular stenosis) and is seen in up to 70% of patients. Other cardiac features include myxomatous degeneration of the aortic or mitral valve leaflets or both, intracardiac lesions like ventricular or atrial septal defects, and early development of hypertension. Cardiac complications are the major cause of death in this syndrome. The major endocrine manifestations include hypercalcemia, subclinical hypothyroidism, and impaired glucose tolerance and diabetes mellitus. Neurological manifestations include global cognitive impairment with characteristic pattern of cognitive strengths in selected language skills and weaknesses in visuospatial skills. Hyperreflexia is more prevalent in lower extremities with poor balance and coordination and up to 10% of patients may have type 1 Chiari malformations. Currently, there is no genetic test that predicts the severity of the WB syndrome phenotype in a given patient. Treatment of the syndrome involves a combination of medical monitoring, anticipatory guidance, direct therapies, pharmacotherapy, surgery, and adaptive changes. None of the available treatments are curative. Surgery is the preferred modality for repair of discrete moderate-severe aortic stenoses. Balloon angioplasty and stent have been tried; however, they carry a higher risk of restenosis, rupture, and aneurysm given the characteristic overgrowth of vascular smooth muscle. Pulmonary artery stenoses may regress over time and are also candidates for angioplasty.
Reviewer's Comments: In my opinion, this is a very nice article summarizing key features in WB syndrome and its management. (Reviewer-Sahil Mehta, MD).

Keywords: Williams–Beuren Syndrome, Supravalvular Aortic Stenosis, Hypercalcemia, Developmental Disorder

Print Tag: Refer to original journal article

What Is the Link Between Hospital Volume, Mortality?

Hospital Volume and 30-Day Mortality for Three Common Medical Conditions.

Ross JS, Normand SL, et al:

N Engl J Med 2010; 362 (March 25): 1110-1118

Admission to a higher volume hospital is associated with lower mortality for the conditions of acute myocardial infarction, congestive heart failure, and pneumonia.

Objective: To investigate the relationship between hospital volumes and their outcomes regarding 3 very common and expensive conditions: myocardial infarction (MI), congestive heart failure (CHF), and pneumonia (PNA).
Methods: The data in this study were obtained using the Medicare administrative claims for acute hospitalizations for MI, CHF, and PNA between 2004 and 2006 in the United States. The analysis for each condition was performed independently. The hospitals were divided into large-, medium-, and small-volume hospitals. Relative effect on the risk-adjusted odds of death within 30 days for increasing increments of 100 patients per hospital was then examined.
Results: The authors identified 734,972 patients for MI, 1,324,287 patients for CHF, and 1,418,252 for PNA. The data indicated that an increased hospital volume was associated with reduced 30-day mortality for all 3 conditions: MI (OR, 0.89; 95% CI, 0.88 to 0.90), CHF (OR, 0.91; 95% CI, 0.90 to 0.92), and PNA (OR, 0.95; 95% CI, 0.94 to 0.96). The mortality benefit, however, became increasingly small and eventually nonsignificant as the volume threshold for each condition was reached. The mortality benefit volume threshold for MI, CHF, and PNA was calculated to be 610, 500, and 210 patients for each condition, respectively. The authors also noted that the volume threshold was lower for the teaching hospitals.
Conclusions: Admission to a higher volume hospital is associated with lower mortality for the conditions of acute MI, CHF, or PNA.
Reviewer's Comments: This study has a number of limitations including: use of administrative records instead of medical records, using only Medicare beneficiary patient population, significant heterogeneity of the patient outcomes, and other confounding factors that affect the hospital volumes not measured in this study. The outcomes of medical procedures have been shown previously to be related to the number of cases performed in each institution. This is one of the few studies that reviews the outcomes of common medical conditions as opposed to surgical procedures. Considering the limitations of this study, the authors do bring attention to the importance of experience and volume in the outcomes of common conditions in different hospitals. Perhaps implementing standard of care protocols for these conditions, especially in low-volume hospitals can improve future patient outcomes. Also, the thresholds provided in this study can be used as a goal for small-volume hospitals to achieve. Regulatory measures can also be taken to avoid small hospitals in close proximity to one another that can dilute the experience of the staff. While there are previous studies that show physician experience and its impact on outcomes, an aggregate of factors such as nursing, emergency, pharmacy, and support staff play a crucial role in patient care. (Reviewer-Behnam Bozorgnia, MD).

Keywords: Common Medical Conditions, Hospital Volume, 30-Day Mortality

Print Tag: Refer to original journal article

Data Fail to Support Continuation of Clopidogrel Past 12 Months Post-DES

Duration of Dual Antiplatelet Therapy After Implantation of Drug-Eluting Stents.

Park SJ, Park DW, et al:

N Engl J Med 2010; March 15 (): epub ahead of print

Among patients treated with drug-eluting stents, continuation of clopidogrel past 12 months may not provide additional benefit over aspirin alone.

Background: Percutaneous coronary intervention (PCI) with drug-eluting stents (DESs) has become the preferred treatment for coronary stenoses given the reduced need for repeat revascularization compared to bare-metal stents (BMSs). Observational studies have shown that early discontinuation of dual antiplatelet therapy (DAT) increases the risk for stent thrombosis leading to myocardial infarction (MI) and death. Current PCI guidelines and the FDA therefore recommend at least 12 months of uninterrupted DAT (most often clopidogrel and aspirin) for patients treated with DES. Whether longer-term DAT is necessary to protect against very late stent thrombosis is not known.
Objective: To evaluate the efficacy of continuation of DAT past 12 months versus aspirin only in patients treated with a DES.
Participants/Methods: Patients from 2 separate randomized trials, REAL-LATE and ZEST-LATE, were included to improve the statistical power of the final analysis since both studies had a similar question and design. The major difference between the 2 studies was that ZEST-LATE included patients from another randomized trial and the study population was limited based on clinical and lesion characteristics. REAL-LATE had a more "real world" population without these exclusions. Patients from either study that remained event-free at 12 months and had no clinical indication for, or contraindication to, the continuation of DAT past 12 months were included. The primary end point was MI or cardiac death. Secondary end points included death from any cause, MI, stroke, TIMI major bleeding, and definite stent thrombosis.
Results: Over approximately 1 year, 2701 patients were randomized (DAT, 1357; aspirin only, 1344) with a median follow-up of 19.2 months. The Kaplan-Meier estimate of event rate for MI or cardiac death at 2 years was 1.8% for DAT and 1.2% for aspirin only (P =0.17). Event rates for secondary end points, including the risk of TIMI major bleeding, were also similar between groups.
Conclusions: There was no significant benefit to continuing DAT past 12 months post-DES when compared with aspirin alone.
Reviewer's Comments: Unfortunately, there were significant limitations to this study. Most importantly, the study was found to be underpowered to detect a difference in MI and cardiac death due to the overall low event rates. Also, this was a Korean study, and the findings may not be applicable to different ethnic groups or places with different interventional practice. This study only looked at the first-generation DESs, and newer-generation DESs may not carry the same risk for stent thrombosis. This study does not support continuation of DAT past 12 months in patients who remain event-free post-DES, but only a larger clinical trial with longer follow-up would truly answer this question. (Reviewer-Parul B. Patel, MD).

Keywords: Dual Antiplatelet Therapy, Drug-Eluting Stents, Thienopyridine

Print Tag: Refer to original journal article

FFR Is 0.78 -- What Next?

Clinical Outcome Following Conservative vs Revascularization Therapy in Patients With Stable Coronary Artery Disease and Borderline Fractional Flow Reserve Measurements.

Lindstaedt M, Halilcavusogullari Y, et al:

Clin Cardiol 2010; 33 (February): 77-83

Coronary artery lesions with fractional flow reserve in the gray zone (0.75 to 0.80) may be safely treated with optimal medical therapy.

Background: Fractional flow reserve (FFR) measures the fraction by which the maximal flow through a coronary artery to the myocardium is reduced by presence of a stenosis. A value of FFR <0.75 is very specific for ischemia and a value >0.80 essentially rules out myocardial ischemia with a sensitivity of 90%. A value between 0.75 and 0.80, the so called "gray zone," presents a dilemma as to treatment options. Most physicians tend to revascularize these lesions to avoid leaving any ischemia untreated. The value of medical treatment versus revascularization in such groups of patients is not known.
Objective: To compare the clinical outcome of these patients with respect to their recommended treatment strategy.
Design/Methods: Retrospective study based on patients selected from a database of 900 consecutive patients in a single center who underwent an FFR measurement as part of routine coronary angiography. Only patients with an FFR value of ≥0.75 and ≤0.80 were included in the study (n=97). Follow-up was done by contacting the patients in the database by telephone and giving them a survey from a detailed questionnaire form, which included assessment of clinical symptoms, hospitalizations, and major adverse cardiac events (MACEs) defined as cardiac death, myocardial infarction (MI), or coronary revascularization with percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG).
Results: At baseline, the group was almost evenly split between medical management (n=48; 49.5%) and revascularization (n=49; 50.5%). Both groups were well matched except for the left anterior descending artery was more frequently assessed in the medical management group and the right coronary artery in the revascularization group. These patients were followed for a mean duration of 24 ± 16 months. There was no difference in survival between groups. MACE rate and hard cardiac events death and myocardial infarction were significantly different, favoring the deferred group. There were 3 cardiac deaths and 6 MIs in the revascularization group. Rehospitalizations were more common in the revascularization group. These results persisted even when the patients undergoing CABG were removed from the analysis.
Conclusions: Patients with coronary artery stenosis with FFR in the grey zone can be safely treated medically without adding additional risk. Moreover, if patients continue to be symptomatic despite maximal medical management, revascularization of these lesions may be considered.
Reviewer's Comments: This retrospective study is interesting in that it provides more data on using FFR for evaluation of coronary artery disease. Revascularizing lesions when FFR is in the grey zone may not be the right option. Larger randomized trials will need to be performed to better define the therapeutic options in such patients. (Reviewer-Pradeep S. Arumugham, MD).

Keywords: Coronary Artery Disease, Physiologic Assessment

Print Tag: Refer to original journal article