

Suggested International Abstracts

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(001)

Byrne MJ, Helm R, Daya S, et al. Diminished Left Ventricular Dyssynchrony and Impact of Resynchronization in Failing Hearts With Right Versus Left Bundle Branch Block.

Objectives: We compared mechanical dyssynchrony and the impact of cardiac resynchronization therapy (CRT) in failing hearts with a pure right (RBBB) versus left bundle branch block (LBBB).

Background: Cardiac resynchronization therapy is effective for treating failing hearts with conduction delay and discoordinate contraction. Most data pertain to LBBB delays. With RBBB, the lateral wall contracts early so that biventricular (BiV) pre-excitation may not be needed. Furthermore, the magnitude of dyssynchrony and impact of CRT in pure RBBB versus LBBB remains largely unknown.

Methods: Dogs with tachypacing-induced heart failure combined with right or left bundle branch radiofrequency ablation were studied. Basal dyssynchrony and effects of single and BiV CRT on left ventricular (LV) function were assessed by pressure-volume catheter and tagged magnetic resonance imaging, respectively.

Results: Left bundle branch block and RBBB induced similar QRS widening, and LV function (ejection fraction, maximum time derivative of LV pressure [dP/dt_{max}]) was similarly depressed in failing hearts with both conduction delays. Despite this, mechanical dyssynchrony was less in RBBB (circumferential uniformity ratio estimate [CURE] index: 0.80 ± 0.03 vs. 0.58 ± 0.09 for LBBB, $p < 0.04$; CURE 0→1 is dyssynchronous→synchronous). Cardiac resynchronization therapy had correspondingly less effect on hearts with RBBB than those with LBBB (i.e., $5.5 \pm 1.1\%$ vs. $29.5 \pm 5.0\%$ increase in dP/dt_{max} , $p < 0.005$), despite similar baselines. Furthermore, right ventricular-only pacing enhanced function and synchrony in RBBB as well or better than did BiV, whereas LV-only pacing worsened function. **Conclusions:** Less mechanical dyssynchrony is induced by RBBB than LBBB in failing hearts, and the corresponding impact of CRT on the former is reduced. Right ventricular-only pacing may be equally efficacious as BiV CRT in hearts with pure right bundle branch conduction delay (J Am Coll Cardiol 2007 50: 1484-1490).

(002)

Schömig A, Dibra A, Windecker S, et al. A Meta-Analysis of 16 Randomized Trials of Sirolimus-Eluting Stents Versus Paclitaxel-Eluting Stents in Patients With Coronary Artery Disease.

Objectives: Our purpose was to make a synthesis of the available evidence on the relative efficacy and safety of 2 drug-eluting stents (DES)—sirolimus-eluting stent (SES) and paclitaxel-eluting stent (PES)—in patients with coronary artery disease.

Background: It is not known whether there are differences in late outcomes between the 2 most commonly used DES: SES and PES.

Methods: Sixteen randomized trials of SES versus PES with a total number of 8,695 patients were included in this meta-analysis. A full set of individual outcome data from 5,562 patients was also available. Mean follow-up period ranged from 9 to 37 months. The primary efficacy end point was the need for reintervention (target lesion revascularization). The primary safety end point was stent thrombosis. Secondary end points were death and recurrent myocardial infarction (MI).

Results: No significant heterogeneity was found across trials. Compared with PES, SES significantly reduced the risk of reintervention (hazard ratio [HR] 0.74; 95% confidence interval [CI] 0.63 to 0.87, $p < 0.001$) and stent thrombosis (HR 0.66; 95% CI 0.46 to 0.94, $p = 0.02$) without significantly impacting on the risk of death (HR 0.92; 95% CI 0.74 to 1.13, $p = 0.43$) or MI (HR 0.84; 95% CI 0.69 to 1.03, $p = 0.10$).

Conclusions: Sirolimus-eluting stents are superior to PES in terms of a significant reduction of the risk of reintervention and stent thrombosis. The risk of death was not significantly different between the 2 DES, but there was a trend toward a higher risk of MI with PES, especially after the first year from the procedure (J Am Coll Cardiol 2007 50: 1373-1380).

(003)

Lee PT, Chou K, Liu C, et al. Renal Protection for Coronary Angiography in Advanced Renal Failure Patients by Prophylactic Hemodialysis: A Randomized Controlled Trial.

Background: Pre-existing renal failure is the greatest risk factor for CN. Hemodialysis can effectively remove contrast media, but its effect upon preventing CN is still uncertain.

Methods: Eighty-two patients with chronic renal failure, referred for coronary angiography, were assigned randomly to receive either normal saline intravenously and prophylactic hemodialysis (dialysis group; $n = 42$) or fluid supplement only (control group; $n = 40$).

Results: Prophylactic hemodialysis lessened the decrease in creatinine clearance within 72 h in the dialysis group (0.4 ± 0.9 ml/min/1.73 m² vs. 2.2 ± 2.8 ml/min/1.73 m²; $p < 0.001$). Compared with the dialysis group, the serum creatinine concentrations in the control group were significantly higher at day 4 (6.3 ± 2.3 mg/dl vs. 5.1 ± 1.3 mg/dl; $p = 0.010$) and at peak level (6.7 ± 2.7 mg/dl vs. 5.3 ± 1.5 mg/dl; $p = 0.005$). Temporary renal replacement therapy was required in 35% of the control patients and in 2% of the dialysis group ($p < 0.001$). Thirteen percent of the control patients, but none of the dialysis patients, required long-term dialysis after discharge ($p = 0.018$). For the patients not requiring chronic dialysis, 13 patients in the control group (37%) and 2 in the dialysis group (5%) had an increase in serum creatinine concentration at discharge of more than 1 mg/dl from baseline ($p < 0.001$).

Conclusions: Prophylactic hemodialysis is effective in

improving renal outcome in chronic renal failure patients undergoing coronary angiography (J Am Coll Cardiol 2007 50: 1015-1020).

(004)

Tivesten A, Mellström D, Jutberger H, et al. Low Serum Testosterone and High Serum Estradiol Associate With Lower Extremity Peripheral Arterial Disease in Elderly Men: The MrOS Study in Sweden.

Objectives: This study sought to determine whether serum levels of testosterone and estradiol associate with lower extremity peripheral arterial disease (PAD) in a large population-based cohort of elderly men.

Background: Few studies have explored the relationship between serum sex steroids and lower extremity PAD in men.

Methods: The Swedish arm of the MrOS (Osteoporotic Fractures in Men) study (n=3,014; average age 75.4 years) assessed ankle-brachial index (ABI) and defined lower extremity PAD as ABI <0.90. Radioimmunoassay measured serum levels of total testosterone, estradiol, and sex hormone-binding globulin, and we calculated free testosterone and free estradiol levels from the mass action equations.

Results: A linear regression model including age, current smoking, previous smoking, diabetes, hypertension, body mass index, free testosterone, and free estradiol showed that free testosterone independently and positively associates with ABI (p<0.001), whereas free estradiol independently and negatively associates with ABI (p<0.001). Logistic regression analyses showed that free testosterone in the lowest quartile (vs. quartiles 2 to 4; odds ratio [OR] 1.65, 95% confidence interval [CI] 1.22 to 2.23, p=0.001) and free estradiol in the highest quartile (vs. quartiles 1 to 3; OR 1.45, 95% CI 1.09 to 1.94, p=0.012) independently associate with lower extremity PAD.

Conclusions: This cross-sectional study shows for the first time that low serum testosterone and high serum estradiol levels associate with lower extremity PAD in elderly men. Future prospective and interventional studies are needed to establish possible causal relationships between sex steroids and the development of lower extremity PAD in men (J Am Coll Cardiol 2007 50: 1070-1076).

(005)

Phillips CO, Kashani A, Ko DK, et al. Adverse Effects of Combination Angiotensin II Receptor Blockers Plus Angiotensin-Converting Enzyme Inhibitors for Left Ventricular Dysfunction. A Quantitative Review of Data From Randomized Clinical Trials.

Background: We performed a meta-analysis of randomized controlled trials to assess ongoing concerns about the safety profile of combination angiotensin II receptor blockers (ARBs) plus angiotensin-converting enzyme (ACE) inhibitors in symptomatic left ventricular dysfunction.

Methods: MEDLINE (January 1966–December 2006) and Web sites for the National Institute of Health Clinical Trials and the Food and Drug Administration were searched for eligible RCTs that included 500 or more subjects, had a follow-up of 3 months or longer, and reported adverse effects. We used a random effects model to calculate the

relative risk (RR) and 95% confidence interval (CI) for the following outcome measures: medication discontinuations because of adverse effects, worsening renal function (an increase in serum creatinine level of 0.5mg/dL [to convert to micromoles per liter, multiply by 88.4]), hyperkalemia (serum potassium level 5.5mEq/L [to convert to millimoles per liter, multiply by 1]), and symptomatic hypotension.

Results: Four studies (N=17 337; mean follow-up, 25 months [range, 11-41 months]) were selected. Combination ARB plus ACE inhibitor vs control treatment that included ACE inhibitors was associated with significant increases in medication discontinuations because of adverse effects in patients with chronic heart failure (RR, 1.38 [95% CI, 1.22-1.55]) or in patients with acute myocardial infarction with symptomatic left ventricular dysfunction (RR, 1.17 [95% CI, 1.03-1.34]), and for both conditions there were significant increases in worsening renal function (RR, 2.17 [95% CI, 1.59-2.97] and RR, 1.61 [95% CI, 1.31-1.98], respectively), hyperkalemia (RR, 4.87 [95% CI, 2.39-9.94] and RR, 1.33 [95% CI, 0.90-1.98], respectively; the latter was not significant), and symptomatic hypotension (RR, 1.50 [95% CI, 1.09-2.07], and RR, 1.48 [95% CI, 1.33-3.18], respectively).

Conclusion: Combination ARB plus ACE inhibitor therapy in subjects with symptomatic left ventricular dysfunction was accompanied by marked increases in adverse effects (Arch Intern Med. 2007;167(18):1930-1936).

(006)

Steven E. Nissen, M.D., and Kathy Wolski, M.P.H. Effect of Rosiglitazone on the Risk of Myocardial Infarction and Death from Cardiovascular Causes.

Background: Rosiglitazone is widely used to treat patients with type 2 diabetes mellitus, but its effect on cardiovascular morbidity and mortality has not been determined.

Methods: We conducted searches of the published literature, the Web site of the Food and Drug Administration, and a clinical-trials registry maintained by the drug manufacturer (GlaxoSmithKline). Criteria for inclusion in our meta-analysis included a study duration of more than 24 weeks, the use of a randomized control group not receiving rosiglitazone, and the availability of outcome data for myocardial infarction and death from cardiovascular causes. Of 116 potentially relevant studies, 42 trials met the inclusion criteria. We tabulated all occurrences of myocardial infarction and death from cardiovascular causes.

Results: Data were combined by means of a fixed-effects model. In the 42 trials, the mean age of the subjects was approximately 56 years, and the mean baseline glycated hemoglobin level was approximately 8.2%. In the rosiglitazone group, as compared with the control group, the odds ratio for myocardial infarction was 1.43 (95% confidence interval [CI], 1.03 to 1.98; P=0.03) and the odds ratio for death from cardiovascular causes was 1.64 (95% CI, 0.98 to 2.74; P=0.06).

Conclusions: Rosiglitazone was associated with a significant increase in the risk of myocardial infarction and with an increase in the risk of death from cardiovascular causes that had borderline significance. Our study was limited by a lack of access to original source data, which would have enabled time-to-event analysis. Despite these limitations, patients and

providers should consider the potential for serious adverse cardiovascular effects of treatment with rosiglitazone for type 2 diabetes (N Engl J med 2007; 356: 2457-2471).

(007)

Kereiakes DK, Teirstein PS, Sarembock IJ, et al. The Truth and Consequences of the COURAGE Trial.

Percutaneous coronary intervention (PCI) has played an integral role in the therapeutic management strategies for patients who present with either acute coronary syndromes or stable angina pectoris. The COURAGE (Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation) trial enrolled patients with chronic stable angina and at least 1 significant ($\geq 70\%$) angiographic coronary stenosis who were randomly assigned to an initial treatment of either PCI in conjunction with optimal medical therapy or optimal medical therapy alone. Although the initial management strategy of PCI did not reduce the risk of death, myocardial infarction, or other major cardiovascular events, improvement in angina-free status and a reduction in the requirement for subsequent revascularization was observed. An in-depth analysis of the COURAGE trial design and execution is provided (J. Am. Coll. Cardiol 2007;50:1598-1603).

(008)

Balkau V, Deanfield JE, Després J, et al. Internatinal Day for the Evaluation of Abdominal Obesity (IDEA): A Study of Waist Circumference, Cardiovascular Disease, and Diabetes Mellitus in 168 000 Primary Care Patients in 63 Countries.

Background: Abdominal adiposity is a growing clinical and public health problem. It is not known whether it is similarly associated with cardiovascular disease (CVD) and diabetes mellitus in different regions around the world, and thus whether measurement of waist circumference (WC) in addition to body mass index (BMI) is useful in primary care practice.

Methods and Results: Randomly chosen primary care physicians in 63 countries recruited consecutive patients aged 18 to 80 years on 2 prespecified half days. WC and BMI were measured and the presence of CVD and diabetes mellitus recorded. Of the patients who consulted the primary care physicians, 97% agreed to participate in the present study. Overall, 24% of 69 409 men and 27% of 98 750 women were obese ($\text{BMI} \geq 30 \text{ kg/m}^2$). A further 40% and 30% of men and women, respectively, were overweight ($\text{BMI} 25$ to 30 kg/m^2). Increased WC (>102 for men and >88 cm for women) was recorded in 29% and 48%, CVD in 16% and 13%, and diabetes mellitus in 13% and 11% of men and women, respectively. A statistically significant graded increase existed in the frequency of CVD and diabetes mellitus with both BMI and WC, with a stronger relationship for WC than for BMI across regions for both genders. This relationship between WC, CVD, and particularly diabetes mellitus was seen even in lean patients ($\text{BMI} < 25 \text{ kg/m}^2$).

Conclusions: Among men and women who consulted primary care physicians, BMI and particularly WC were both strongly linked to CVD and especially to diabetes mellitus. Strategies to address this global problem are required to prevent an epidemic of these major causes of morbidity and mortality (Circulation. 2007;116:1942-1951).

(009)

Mazzei V, Nasso G, Salamone G, et al. Prospective Randomized Comparison of Coronary Bypass Grafting With Minimal Extracorporeal Circulation System (MECC) Versus Off-Pump Coronary Surgery.

Background: We aimed to evaluate the clinical results and biocompatibility of the minimal extracorporeal circulation system (MECC) compared with off-pump coronary revascularization (OPCABG).

Methods and Results: In a prospective randomized study, 150 patients underwent coronary surgery with the use of MECC and 150 underwent OPCABG. End points were (1) circulating markers of inflammation and organ injury, (2) operative results, and (3) outcome at 1-year follow up. Operative mortality and morbidity were comparable between the groups. Release of inflammatory markers was similar between groups at all time points (peak interleukin-6 167.2 ± 13.5 versus 181 ± 6.5 pg/mL, $P=0.14$, OPCABG versus MECC group, respectively). Peak creatine kinase was 419.3 ± 103.5 versus 326 ± 84.2 mg/dL ($P=0.28$), and peak S-100 protein was 0.13 ± 0.08 versus 0.29 ± 0.1 pg/mL ($P=0.058$, OPCABG versus MECC group, respectively). Length of hospital stay and use of blood products were similar between groups. Two cases of angina recurrence at 1 year in the MECC group were observed versus 5 cases observed in the OPCABG group ($P=0.44$). A residual perfusion defect at myocardial nuclear scan was less frequent among patients in the MECC group (3 versus 9 cases, $P=0.14$; odds ratio 0.32, 95% confidence interval 0.07 to 1.32). Six (OPCABG group) versus 3 (MECC group) coronary grafts were occluded or severely stenotic at 1 year ($P=0.33$, odds ratio 0.47, 95% confidence interval 0.09 to 2.14).

Conclusions: Clinical results of coronary revascularization with MECC are optimal when this procedure is performed by experienced teams. Postoperative morbidity is comparable to that with OPCABG. MECC is associated with little pump-related systemic and organ injury. It may achieve the benefits of OPCABG (less morbidity in high-risk patients) while facilitating complete revascularization in the case of complex lesions unsuitable for OPCABG (Circulation. 2007;116:1761-1767).

(010)

Svennevig JL, Abdelnoor M, and Hauge S. Twenty-Five-Year Experience With the Medtronic-Hall Valve Prosthesis in the Aortic Position: A Follow-Up Cohort Study of 816 Consecutive Patients.

Background: The Medtronic-Hall valve was developed and for the first time implanted in Oslo, Norway, in 1977. A total of 1104 patients received this valve at Rikshospitalet from 1977 to 1987. In the present study, we followed up on all 816 patients undergoing aortic valve replacement over a 25-year period.

Methods and Results: This is a retrospective cohort analysis of 816 consecutive patients undergoing aortic valve replacement with the Medtronic-Hall valve at Rikshospitalet, Oslo, Norway, from 1977 to 1987. All patients were contacted by means of questionnaires or telephone. Data were checked against hospital databases and medical records. Date of death was verified by the Norwegian civil registry.

Follow-up was 99.6% complete. Survival analysis included operative deaths as well as late deaths. Survival at 25 years was 24.9%. No mechanical failures were found. Valve thrombosis was seen in 4 patients, in 1 case combined with pannus formation. Small valves (20 mm to 21 mm) were associated with reduced survival; however, when controlled for the confounding effects of age and gender, valve size did not remain a significant risk factor. Patient-related factors were important: Older age, female gender, and the need for

concomitant coronary artery bypass surgery significantly reduced survival, whereas surgery of the ascending aorta did not. Linearized rates of thromboembolic complications, warfarin-related bleeding, and endocarditis were 1.5%, 0.7%, and 0.16%/patient-year, respectively. At follow-up, 79% of the patients were in New York Heart Association classes I to II. **Conclusions:** This study confirms the excellent long-term outcome for patients with Medtronic-Hall valves in the aortic position (Circulation. 2007;116:1795-1800).