

The RAPID by UCLA IM Residents

Rapid Access to Prioritized Information and Data

1. Lower targets in diabetes

Howard BV, Roman MJ, Devereux RB et al. Effect of lower targets for blood pressure and LDL cholesterol on atherosclerosis in diabetes: the SANDS randomized trial. JAMA 2008 Apr 9;299(14):1678-89

CONTEXT: Individuals with diabetes are at increased risk for cardiovascular disease (CVD), but more aggressive targets for risk factor control have not been tested. **OBJECTIVE:** To compare progression of subclinical atherosclerosis in adults with type 2 diabetes treated to reach aggressive targets of low-density lipoprotein cholesterol (LDL-C) of 70 mg/dL or lower and systolic blood pressure (SBP) of 115 mm Hg or lower vs standard targets of LDL-C of 100 mg/dL or lower and SBP of 130 mm Hg or lower.

DESIGN, SETTING, AND PARTICIPANTS: A randomized, open-label, blinded-to-end point, 3-year trial from April 2003-July 2007 at 4 clinical centers in Oklahoma, Arizona, and South Dakota. Participants were 499 American Indian men and women aged 40 years or older with type 2 diabetes and no prior CVD events. **INTERVENTIONS:** Participants were randomized to aggressive (n=252) vs standard (n=247) treatment groups with stepped treatment algorithms defined for both. **MAIN**

OUTCOME MEASURES: Primary end point was progression of atherosclerosis measured by common carotid artery intimal medial thickness (IMT). Secondary end points were other carotid and cardiac ultrasonographic measures and clinical events.

RESULTS: Mean target LDL-C and SBP levels for both groups were reached and maintained. Mean (95% confidence interval) levels for LDL-C in the last 12 months were 72 (69-75) and 104 (101-106) mg/dL and SBP levels were 117 (115-118) and 129 (128-130) mm Hg in the aggressive vs standard groups, respectively. Compared with baseline, IMT regressed in the aggressive group and progressed in the standard group (-0.012 mm vs 0.038 mm; $P < .001$); carotid arterial cross-sectional area also regressed (-0.02 mm² vs 1.05 mm²; $P < .001$); and there was greater decrease in left ventricular mass index (-2.4 g/m^{2.7}) vs -1.2 g/m^{2.7}; $P = .03$) in the aggressive group. Rates of adverse events (38.5% and 26.7%; $P = .005$) and serious adverse events (n = 4 vs 1; $P = .18$) related to blood pressure medications were higher in the aggressive group. Clinical CVD events (1.6/100 and 1.5/100 person-years; $P = .87$) did not differ significantly between groups.

CONCLUSIONS: Reducing LDL-C and SBP to lower targets resulted in regression of carotid IMT and greater decrease in left ventricular mass in individuals with type 2 diabetes. Clinical events were lower than expected and did not differ significantly between groups. Further follow-up is needed to determine whether these improvements will result in lower long-term CVD event rates and costs and favorable risk-benefit outcomes.

**Comment from nominator: More evidence for tighter control, although no mortality data presented. Only indirect endpoints measured.*

2. Statins in the elderly with CHD

Afilalo J, Dugue G, Steele R et al. Statins for secondary prevention in elderly patients: a hierarchical Bayesian meta-analysis. J Am Coll Cardiol. 2008 Jan 1;51(1):37-45

OBJECTIVES: This study was designed to determine whether statins reduce all-cause mortality in elderly patients with coronary heart disease.

BACKGROUND: Statins continue to be underutilized in elderly patients because evidence has not consistently shown that they reduce mortality. **METHODS:** We searched 5 electronic databases, the Internet, and conference proceedings to identify relevant trials. In addition, we obtained unpublished data for the elderly patient subgroups from 4 trials and for the secondary prevention subgroup from the PROSPER (PROspective Study of Pravastatin in the Elderly at Risk) trial. Inclusion criteria were randomized allocation to statin or placebo, documented coronary heart disease, ≥ 50 elderly patients (defined as age ≥ 65 years), and ≥ 6 months of follow-up. Data were analyzed with hierarchical Bayesian modeling. **RESULTS:** We included 9 trials encompassing 19,569 patients with an age range of 65 to 92 years. Pooled rates of all-cause mortality were 15.6% with statins and 18.7% with placebo. We estimated a relative risk reduction of 22% over 5 years (relative risk [RR] 0.78; 95% credible interval [CI] 0.65 to 0.89). Furthermore, statins reduced coronary heart disease mortality by 30% (RR 0.70; 95% CI 0.53 to 0.83), nonfatal myocardial infarction by 26% (RR 0.74; 95% CI 0.60 to 0.89), need for revascularization by 30% (RR 0.70; 95% CI 0.53 to 0.83), and stroke by 25% (RR 0.75; 95% CI 0.56 to 0.94). The posterior median estimate of the number needed to treat to save 1 life was 28 (95% CI 15 to 56).

CONCLUSIONS: Statins reduce all-cause mortality in elderly patients and the magnitude of this effect is substantially larger than had been previously estimated

3. Chemoembolization + RFA is better than alone

Cheng BQ, Jia CQ, Liu CT et al. Chemoembolization combined with radiofrequency ablation for patients with hepatocellular carcinoma larger than 3cm: a randomized controlled trial. JAMA 2008 Apr 9;299(14):1669-77

CONTEXT: Transarterial chemoembolization (TACE) combined with radiofrequency ablation (RFA) therapy has been used for patients with large hepatocellular carcinoma tumors, but the survival benefits of combined treatment are not known.

OBJECTIVE: To compare rates of survival of patients with large hepatocellular carcinoma tumors who received treatment with TACE combined with RFA therapy (TACE-RFA), TACE alone, and RFA alone.

DESIGN, SETTING, AND PATIENTS: Randomized controlled trial conducted from January 2001 to May 2004 among 291 consecutive patients with hepatocellular carcinoma larger than 3 cm at a single center in China. **INTERVENTION:** Patients were randomly assigned to treatment with combined TACE-RFA (n = 96), TACE alone (n = 95), or RFA alone (n = 100). **MAIN**

OUTCOME MEASURES: The primary end point was survival

and the secondary end point was objective response rate.

RESULTS: During a median 28.5 months of follow-up, median survival times were 24 months in the TACE group (3.4 courses), 22 months in the RFA group (3.6 courses), and 37 months in the TACE-RFA group (4.4 courses). Patients treated with TACE-RFA had better overall survival than those treated with TACE alone (hazard ratio [HR], 1.87; 95% confidence interval [CI], 1.33-2.63; $P < .001$) or RFA (HR, 1.88; 95% CI, 1.34-2.65; $P < .001$). In a preplanned stratification analysis, survival was also better in the TACE-RFA group than in the RFA group for patients with unimodular hepatocellular carcinoma (HR, 2.50; 95% CI, 1.42-4.42; $P = .001$) and in the TACE-RFA group than the TACE group for patients with multinodular hepatocellular carcinoma (HR, 1.99; 95% CI, 1.31-3.00; $P < .001$). The rate of objective response sustained for at least 6 months was higher in the TACE-RFA group (54%) than with either TACE (35%; rate difference, 0.19; 95% CI, 0.06-0.33; $P = .009$) or RFA (36%; rate difference, 0.18; 95% CI, 0.05-0.32; $P = .01$) treatment alone.

CONCLUSION: In this patient group, TACE-RFA was superior to TACE alone or RFA alone in improving survival for patients with hepatocellular carcinoma larger than 3 cm.

7. Risk of infection in Femoral vs. IJ catheterization

Parietti JJ, Thirion M, Megarbane B. et al. Femoral vs. jugular venous catheterization and risk of nosocomial events in adults requiring acute renal replacement: a randomized controlled trial. *JAMA* 2008 May 28;299(20):2413-22

CONTEXT: Based on concerns about the risk of infection, the jugular site is often preferred over the femoral site for short-term dialysis vascular access. **OBJECTIVE:** To determine whether jugular catheterization decreases the risk of nosocomial complications compared with femoral catheterization. **DESIGN, SETTING, AND PATIENTS:** A concealed, randomized, multicenter, evaluator-blinded, parallel-group trial (the Cathedia Study) of 750 patients from a network of 9 tertiary care university medical centers and 3 general hospitals in France conducted between May 2004 and May 2007. The severely ill, bed-bound adults had a body mass index (BMI) of less than 45 and required a first catheter insertion for renal replacement therapy. **INTERVENTION:** Patients were randomized to receive jugular or femoral vein catheterization by operators experienced in placement at both sites. **MAIN OUTCOME MEASURES:** Rates of infectious complications, defined as catheter colonization on removal (primary end point), and catheter-related bloodstream infection. **RESULTS:** Patient and catheter characteristics, including duration of catheterization, were similar in both groups. More hematomas occurred in the jugular group than in the femoral group (13/366 patients [3.6%] vs 4/370 patients [1.1%], respectively; $P = .03$). The risk of catheter colonization at removal did not differ significantly between the femoral and jugular groups (incidence of 40.8 vs 35.7 per 1000 catheter-days; hazard ratio [HR], 0.85; 95% confidence interval [CI], 0.62-1.16; $P = .31$). A prespecified subgroup analysis demonstrated significant qualitative heterogeneity by BMI (P for the interaction term $< .001$). Jugular catheterization significantly increased incidence of catheter colonization vs femoral catheterization (45.4 vs 23.7 per 1000 catheter-days; HR, 2.10;

95% CI, 1.13-3.91; $P = .017$) in the lowest tercile (BMI < 24.2), whereas jugular catheterization significantly decreased this incidence (24.5 vs 50.9 per 1000 catheter-days; HR, 0.40; 95% CI, 0.23-0.69; $P < .001$) in the highest tercile (BMI > 28.4). The rate of catheter-related bloodstream infection was similar in both groups (2.3 vs 1.5 per 1000 catheter-days, respectively; $P = .42$).

CONCLUSION: Jugular venous catheterization access does not appear to reduce the risk of infection compared with femoral access, except among adults with a high BMI, and may have a higher risk of hematoma.

***Comment from nominator: concealed, randomized, multicenter prospective, evaluator-blinded parallel group trial-- high lines don't reduce risk of infection compared to fem lines. rate of hematoma formation is higher in high lines. Higher BMI people have a higher rate of fem catheter colonization whereas thinner ppl have a higher rate of high line colonization.*

New medications and treatments

Bevacizumab (Avastin) – a recombinant humanized monoclonal Ab that binds to VEGF-receptor is now approved by FDA as first line agent for HER-2 negative metastatic breast cancer when given as combination regimen with paclitaxel – previously only approved for metastatic colon cancer, and metastatic non-small cell lung cancer.

Increased progression free survival ~6months, but no overall survival benefit in 722 patients. Adverse effect include fatigue, nausea, HTN, headache. Cost is high: \$9625/month. Genentech has pt assistance program for income $< \$100,000$, provides for free after 10,000mg taken = \$ 68,700.

Updated Guidelines

Task force recommends diabetes screening in adults with high blood pressure

The U.S. Preventive Services Task Force, in an updated recommendations statement, says that physicians should screen for type 2 diabetes in asymptomatic adults with sustained blood pressure (either treated or untreated) greater than 135/80 mm Hg. The USPSTF concludes that for adults with blood pressure of 135/80 or less, evidence of the value of screening for diabetes is lacking and the balance of benefits and harms cannot be determined.

In the News/Unpublished Data

Measles outbreak in the US - since Jan to May 2008, 64 cases of measles have been reported (63/64 were unvaccinated) in CA, AZ, MI, WI, NY, PA, HI, and VA. 54 cases associated with importation of disease. Should vaccinate all > 12 months old with no e/o immunity (not born before 1957, no convincing h/o clinical measles, no documentation of vaccination and no laboratory e/o immunity) should be vaccinated with MMR or monovalent measles vaccine – attenuated live-virus vaccine. Contraindications: pregnancy, immunosuppressive tx, leukemia/lymphoma, congenital/acquired immunodeficiency.