ON-PUMP VERSUS OFF-PUMP CABG IN HIGH-RISK PATIENTS EUROSCORE 6+ [PRAGUE6] STUDY

The PRAGUE 6 trial [NCT00606372] results indicated that off-pump surgery in high-risk patients is associated with a lower incidence of serious complications and is a safer way of direct revascularization in these patients. Jan Hlavicka, MD, Kralovske Vinohrady University Hospital, Prague, Czech Republic, presented the findings of this prospective, randomized, single center, intention-to-treat assessment study.

The primary endpoint was the composite of death, MI, stroke, and new renal failure requiring hemodialysis at 30 days post operation. Patients were mean age 74 years with a mean additive EuroSCORE (Table 1) of 7.7; approximately 64% of the 206 enrolled patients had a recent MI. A total of 206 patients were randomly assigned to off-pump (n=98) or on-pump CABG (n=108).

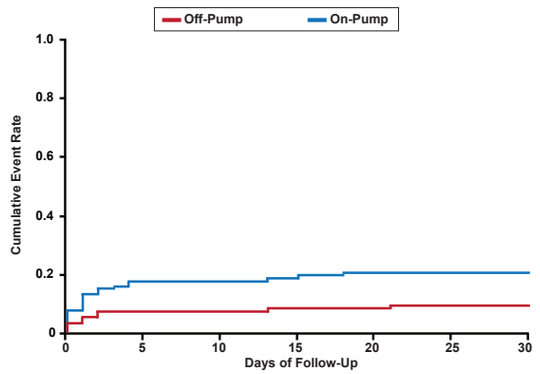
Table 1. EuroSCORE Risk Assessment Criteria

Factors	Score
Patient-related factors	
Age	1
Sex	1
Chronic pulmonary disease	1
Extracardiac arteriopathy	2
Neurological dysfunction	2
Previous cardiac surgery	3
Serum creatinine	2
Active endocarditis	3
Critical preoperative state	3
Cardiac-related factors	
Unstable angina	2
Left ventricular dysfunction Preop EF 30%-50% Preop EF <30%	 1 3
Recent myocardial infarct	2
Pulmonary hypertension	2
Surgical-related factors	
Emergency	2
Other than isolated CABG	2
Surgery on thoracic aorta	3
Postinfarct septal rupture	4

CABG=coronary artery bypass grafting; EF=ejection fraction.

At 30 days, the primary composite endpoint was significantly lower in the off-pump (9.2%) versus on-pump group (20.6%; HR, 0.41; 95% CI, 0.19 to 0.91; p=0.028; Figure 1), driven exclusively by a nearly 3-fold increase in the rate of MI between the off-pump and on-pump groups (4.1% vs 12.1%; HR, 0.32; 95% CI, 0.11 to 0.99; p=0.048). Off-pump patients tended to have a lower incidence of secondary endpoints (eg, need for red blood cell transfusion and re-exploration for bleeding or tamponade). Study limitations included the small number of patients, single-center design, use of only 5 surgeons, and short-term (30-day follow-up) results.

Figure 1. Incidence of Combined Primary Endpoint During First 30 Days



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Taken together, the conflicting results of these 3 studies (2 showed no difference, 1 favored off-pump CABG) indicate a need for larger, well-controlled studies with longer follow-up. Of particular interest is whether there are patients for whom one approach may be safer than the other.

HPS2-THRIVE: Niacin Fails to Show Benefit in Patients at High Risk of Vascular Events

Written by **Phil Vinall**

The results of this large randomized controlled trial in patients with well-controlled lipid levels but who are at a high risk of cardiovascular events once again call into question the the clinical benefits of niacin despite an increase in high-density lipoprotein cholesterol (HDL-C), and reductions in triglyceride levels and low density lipoprotein cholesterol (LDL-C) levels. Jane M. Armitage, MD, Oxford University, Oxford, United Kingdom, presented the results of the Treatment of HDL to Reduce the Incidence of Vascular Events trial [HPS2-THRIVE Collaborative Group. *Eur Heart J* 2013]. Prof. Armitage reported that adding extended-release niacin plus laropiprant (ERN/LRPT), an antiflushing agent, to background therapy with simvastatin (with or without ezetimibe) did not reduce the risk of heart attack, stroke, and revascularizations, and was associated with significantly increased serious adverse events (SAEs).

HPS2-THRIVE randomized 25,673 patients from China, United Kingdom, and Scandinavia with a prior history of myocardial infarction (MI), ischemic stroke or transient ischemic attack, peripheral arterial disease, or diabetes with other cardiovascular disease, on a background

of simvastatin with or without ezetimibe, to either ERN 2 g plus LRPT 40 mg daily (n=12,838) or placebo (12,835). Lipid stabilization was achieved prerandomization using simvastatin 40 mg daily (with or without ezetimibe) to target total cholesterol of 135 mg/dL and patients were followed for 4 years. The primary endpoint was time to first major vascular event, defined as a nonfatal MI or coronary death, nonfatal or fatal stroke, or revascularization. Mean baseline total cholesterol, direct-LDL, HDL, and triglycerides levels were 128, 63, 44, and 125 mg/dL, respectively, which were below the targets for such high-risk patients.

By the end of the 4-year study, 25% of the ERN/LRPT and 17% of the placebo-treated patients had discontinued study treatment and the average overall compliance with ERN/LRPT was 78%. SAEs, including new-onset diabetes, occurred significantly more often in the ERN/LRPT group versus placebo (Table 1). In addition, myopathy was more common in the ERN/LPRT arm (0.6%) versus placebo (0.1%; 95% CI, 2.62 to 7.50; p<0.0001) and much higher in China than in Europe (0.13%/year vs 0.04%/year; p=0.001).

Table 1. SAEs With ERN/LRPT

SAE	ERN/LRPT (n=12,838)	Placebo (n=12,835)	Risk Ratio (95% CI)
Diabetes			
Any diabetic complication[1]	460 (11.1)	311 (7.5)	1.55 (1.34 – 1.78)
New onset diabetes[2]	792 (9.1)	632 (7.3)	1.27 (1.14 – 1.41)
Infections	1031 (8.0)	853 (6.6)	1.22 (1.12 – 1.34)
Gastrointestinal	620 (4.8)	491 (3.8)	1.28 (1.13 – 1.44)`
Bleeding (any)	326 (2.5)	238 (1.9)	1.38 (1.17 – 1.62)
Musculoskeletal	481 (3.7)	385 (3.0)	1.26 (1.10 – 1.44)
Skin[3]	86 (0.7)	51 (0.4)	1.67 (1.20 – 2.34)

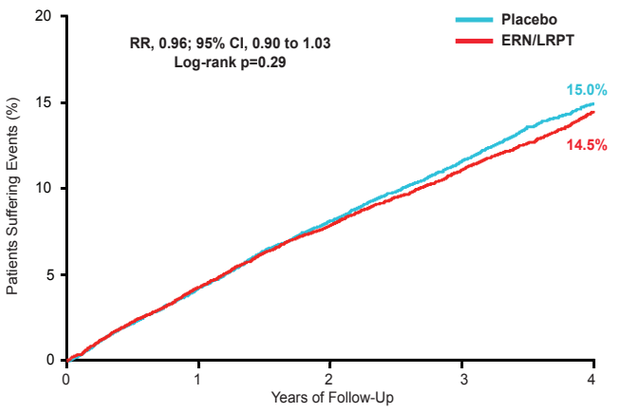
ERN/LRPT=extended-release niacin plus laropiprant; SAE=serious adverse event.

[1]Among participants with diabetes at randomization (n=8299); [2]Among participants without diabetes at randomization (n=17,374); [3]Skin = rash, ulcer, other

On average, treatment with ERN/LRPT decreased LDL-C by 10 mg/dL and triglycerides by 33 mg/dL, while increasing HDL-C by 6 mg/dL. There was no significant reduction in the primary endpoint (major coronary event, stroke, or revascularization) with ERN/LRPT compared with placebo after 4 years (14.5% vs 15.0%, RR, 0.96; 95% CI, 0.90 to 1.03; p=0.29; Figure 1).

There was an overall significant reduction in revascularizations with ERN/LRPT versus placebo (revascularization events, 6.3% vs 7.0%; p=0.03) with no significant differences in any of the other components of the primary endpoint, including coronary death, nonfatal MI, ischemic stroke, or hemorrhagic stroke. All-cause death tended to occur more frequently with ERN/LRPT than placebo (6.2% vs 5.7%; RR, 1.09; 95% CI, 0.99 to 1.21; p=0.08).

Figure 1. Effect of ERN/LRPT on Major Vascular Events



ERN/LRPT=extended-release niacin plus laropiprant.

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There were no significant differences in any of the subgroup comparisons based on age, sex, baseline disease category, or type of statin-based therapy, except for an excess of statin-related myopathy in Chinese patients.

The findings of HPS-THRIVE are consistent with those of previous niacin trials, including AIM-HIGH [AIM-HIGH Investigators. *N Engl J Med* 2011], and suggest lack of clinical benefit with niacin in the treatment and prevention of cardiovascular disease among patients receiving statin therapy. Whether other therapies (eg, CETP inhibitors, PCSK9 inhibitors) that increase HDL-C and/or lower LDL-C may be beneficial in addition to statins are being explored in ongoing Phase 3 trials.

High-Dose Rosuvastatin Reduces Contrast-Induced Nephropathy

Written by Phil Vinall

Among statin-naïve patients with non-ST-segment elevation acute coronary syndrome (NSTE-ACS) managed with an early invasive strategy, pretreatment with high-dose rosuvastatin was associated with a significant reduction in the incidence of contrast-induced acute kidney injury (CI-AKI). In addition, pretreatment with rosuvastatin was also associated with a reduction in adverse clinical events at 30 days compared with placebo. Anna Toso, MD, Misericordia e Dolce Hospital, Prato, Italy, presented the results of the Protective Effect of Rosuvastatin and Antiplatelet Therapy on Contrast-Induced Acute Kidney Injury and Myocardial Damage in Patients With Acute Coronary Syndrome study [PRATO-ACS; NCT01185938] on behalf of the trial investigators.