Long-term follow-up of the PURE study is ongoing. Future reports from the PURE trial will examine specific barriers to effective health care delivery, with the intention of shaping national policies to increase access to medications that are vital for the secondary prevention of CVD.

The results of this large global study underscore the importance of efforts to increase the use of proven secondary preventive therapies and offer an opportunity to reduce CV morbidity and mortality using proven, available, and inexpensive therapies. While the greatest need appears to be in lower-income countries, there appears to be significant underuse in high-income countries as well. These data support the concept of a "polypill," which has the potential to deliver multiple proven therapies in a single pill in an attempt to close the large treatment gap that was observed in this analysis. The appeal of such an approach is the simplicity that it offers to deliver several drugs at once, which may outweigh the limited flexibility in the selection of the specific drugs and their doses.

Additional reading: Yusuf S et al. *Lancet* 2011.

Postprandial TG and Risk in Patients with CVD

Written by Anne Jacobson

The Homburg Cream and Sugar Study (HCS) provided additional information regarding the relationship of fasting and postprandial triglyceride (TG) levels and risk in patients with cardiovascular disease (CVD). The study was designed to determine whether the measurement of postprandial TG levels improved risk prediction of cardiovascular (CV) events over traditional risk markers in stable patients with CVD. Risk prediction using fasting serum TG in high-risk patients with normal impaired glucose tolerance remains uncertain. The role of postprandial serum TGs as a risk modifier in secondary prevention is unknown. Ulrich Laufs, MD, Universitätsklinikum des Saarlandes, Homburg, Germany, discussed the results of the prospective HCS study [NCT00628524].

A long-standing association exists between elevated TG levels and CVD [Miller M et al. *Circulation* 2011; Sarwar N et al. *Circulation* 2007; Austin MA et al. *Am J Cardiol* 1998]. However, the extent to which TG directly promotes CVD or represents an independent biomarker of risk has been debated for decades [Hulley SB et al. *N Eng J Med* 1980]. Serum concentrations of TG-rich lipoproteins are strongly correlated with the time and the type of food intake and therefore the within patient variability is large. In addition, concomitant metabolic factors such as insulin resistance and genetic predisposition affect the individual fasting TG and postprandial TG kinetics. Impaired glucose tolerance and diabetes remain undiagnosed in a significant proportion of patients which may be important for the epidemiologic association of TG with CVD. HCS is the first study that determines glucose tolerance and postprandial TGs concurrently in a larger cohort of individuals.

Basic science suggests that nonfasting TG may correlate more closely with atherogenic remnant lipoprotein particles. Hydrolysis of the postprandial TG-rich lipoproteins yields small cholesterol-enriched remnant lipoprotein particles that have been shown to exert atherogenic effects and the lipolysis of TG-rich lipoproteins along the vessel wall producing potentially toxic oxidized fatty acids. The concept that atherosclerosis was a postprandial phenomenon was suggested many years ago. Subgroup analyses of the Copenhagen City Heart Study and the Women's Health Study found that nonfasting TGs represent a superior predictor of incident CVD compared with fasting levels in primary prevention [Jackson KG et al. *Atherosclerosis* 2011].

The HCS study was therefore designed to determine whether characterization of postprandial TG kinetics may improve the prediction of CV events in addition to the assessment of glucose tolerance and traditional risk factors. The researchers developed an oral TG and glucose tolerance test to obtain standardized measurements of postprandial TG kinetics in 514 consecutive patients with angiographically confirmed coronary artery disease (CAD). Follow-up was 18 months, and the primary outcome was the composite of CV death and CV hospitalization, a broad endpoint that included hospitalization for acute coronary syndromes, unplanned (symptom-driven) coronary angiography, heart failure, ischemic stroke or transient ischemic attack, cardiac arrhythmia that required resuscitation, and unplanned cardiac device implantation.

Findings indicated that postprandial TG kinetics depended on glucose tolerance. Patients with normal glucose tolerance had lower fasting TG (n=126; mean TG 108±42 mg/dL) and a lower absolute postprandial TG increase compared with patients with pathological glucose metabolism (n=388; mean fasting TG 172±157 mg/dL), whereas the mean relative TG increase was similar.

Overall, postprandial TG level was not associated with CV risk (p=NS). Fasting TG level was associated with risk in univariate analysis; however, after adjustment, this relationship was no longer significant (p=NS).

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In subgroup analyses, neither postprandial TG level nor fasting TG level was associated with outcome in patients with impaired glucose tolerance. In the subgroup of patients with normal glucose metabolism, however, fasting TG as well as postprandial TG kinetics (area under the curve and the relative postprandial increase) was associated with the primary endpoint. They remained independent predictors in those patients in the highest tertile of TG versus the lowest after adjustment for baseline characteristics, metabolic parameters, and CV risk factors (fasting TG >150 mg/dL vs <106 mg/dL; HR, 3.10; 95% CI, 1.06 to 9.06; p=0.04; relative postprandial TG increase >210% vs <171%; HR, 4.45; 95% CI, 1.33 to 14.91; p=0.02).

The outcomes that were observed in the subgroup with normal glucose tolerance are generally consistent with a recently released scientific statement from the American Heart Association [Miller M. *Circulation* 2011], which states that TG levels appear to provide unique information as a biomarker of risk, especially when combined with low high-density lipoprotein cholesterol and elevated low-density lipoprotein cholesterol. The statement acknowledges the pivotal role that TG plays in lipid metabolism and reaffirms that it is not directly atherogenic due to its association with atherogenic remnant particles and apo CIII.

While overall this study did not show an association between postprandial TG level and outcome after adjustment for known risk factors, the authors noted that there is an association with CV events in the subgroup of patients with CAD and normal glucose tolerance. Commenting on the findings, Prof. Laufs observed, "It seems that glucose tolerance determines triglyceride pharmacokinetics." Fasting and postprandial TG values independently predicted CV events in patients with CAD and normal glucose tolerance.

Several important aspects of this trial should be noted when applying these findings in clinical practice, including a modest cohort size, a high rate of statin use (95%), a broad primary endpoint that includes diverse outcomes that may or may not be modified by TG level, and the use of a specific protocol for TG and glucose tolerance assessment. The interesting relationship of TG and outcomes in the subgroup of patients with normal glucose tolerance should be confirmed by independent outcome studies, though HCS is by far the largest study using a comprehensive metabolic test protocol to date. In summary, fasting TGs and – with superior risk prediction – postprandial TGs correlate with CV events in patients with CAD and normal glucose tolerance but do not independently predict CV outcomes in patients with impaired glucose metabolism.

EXAMINATION: Similar Outcomes with New-Generation DES Compared with BMS for Patients with Acute STEMI Undergoing PCI

Written by Anne Jacobson

For patients with acute ST elevation myocardial infarction (STEMI), outcomes with percutaneous coronary intervention (PCI) using a new-generation drug-eluting stent (DES) were similar after 1 year compared with a bare-metal stent (BMS), according to new findings from the Evaluation of Xience V Stent in Acute Myocardial Infarction trial [EXAMINATION; NCT00828087].

Manel Sabaté, MD, University Hospital Clinic, Barcelona, Spain, presented results from the multinational EXAMINATION study.

EXAMINATION included 1504 patients who presented with STEMI within 48 hours of symptom onset. All patients required emergent PCI and were required to have a target vessel diameter of 2.25 to 4.0 mm to accommodate currently available stents. The "all-comer" trial design resulted in a study population that was highly representative of real-world patients who are undergoing PCI for acute STEMI. The study enrolled 70% of all STEMI patients who presented to 12 study sites in Spain, Italy, and The Netherlands, including patients who presented within 12 hours of symptom onset (primary PCI), after successful thrombolysis, after failed thrombolysis (rescue PCI), and between 12 and 48 hours of symptom onset (latecomers).

Patients were randomly assigned, in a single-blind fashion, to intervention with an everolimus-eluting stent (EES; n=751) or a cobalt-chromium stent (n=747). Baseline and procedural characteristics were similar in the two treatment groups, including good compliance with antithrombotic medications at discharge and throughout the 1-year follow-up period (approximately 90% was on dual antiplatelet therapy [DAPT] at 1 year). Acute procedure-related outcomes were similar in the DES and BMS groups, with a low risk of TIMI bleeding and very low rate of device malfunction (0.5% vs 0.7%; p=NS). The primary composite endpoint was all-cause death, myocardial infarction (MI), and revascularization. The trial, as designed, had 86% power to detect a 30% reduction in the rate of the primary endpoint at 1 year for DES compared with BMS.

After 1 year, a similar proportion of patients in the DES and BMS groups remained free from the primary endpoint (87.8% vs 85.7%; p=0.20). Several individual endpoints were