How well are CEE health care providers managing LDL-cholesterol?

The DA-VINCI study aimed to evaluate the lipid management strategies of Central and Eastern European (CEE) health care providers. Over the last 20 years, economic advancements have improved healthcare in CEE, reflected by reductions in CVD mortality and morbidity. The countries included in this evaluation, the Czech Republic, Hungary, Poland, Romania, Slovakia, and Ukraine, have adopted the 2016 and 2019 European Society of Cardiology (ESC)/European Atherosclerosis Society (EAS) guidelines. How well are these guidelines implemented, and are patients in a primary and a secondary prevention setting reaching the recommended LDL-c goals? This cross-sectional observational study was
done between June 2017 and November 2019 (N=2154). Majority of the included patients used moderate (53%) or high intensity (32%) statins. The ESC/EAS recommended LDL-c targets were reached by 21% (Ukraine) - 50% (Hungary and Romania) of the patients. The more stringent 2019 ESC/EAS LDL-c targets were achieved by 24% of the overall population (11% in Ukraine – 32% in Poland). These findings underline the significant gap between guideline-recommended targets vs. the reality of clinical practice. Three-quarters of the participants failed to attain evidence-based LDL- recommendations and remained exposed to an avoidable increased risk of first or recurrent ASCVD events. Strategies to improve cholesterol management are urgently warranted to ensure a downward curve of ASCVD morbidity and mortality in CEE countries.


**The impact of combining statins + ezetimibe in a single pill vs. a two-pill regimen**

Managing LDL-c according to recent guidelines has become more challenging, whereby mono-therapy, similar as in hypertension management, is unlikely to enable patients to reach the updated LD-c targets. Adherence to medication that enables patients to lower their plasma LDL-c levels is notoriously poorly accepted. This retrospective observational study evaluated 256 012 patients from the Lombardy region in Italy to compare adherence to a single pill (N=5351) vs. a two-pill (N=2881) combination of statin + ezetimibe. The adherence was measured after 1-year as the proportion of days covered (PDC). This is the ratio between the number of days the drug was available and the days of follow-up. A PDC of > 75% was labeled as highly adherent and a PDC < 35 as poorly adherent to drug therapy. Patients that were prescribed a single pill had an 87% (75–99%) greater odds of being highly adherent and a 79% (72–84%) lower odds of being poorly adherent. Impressive was the noted 55% reduction in ASCVD events in highly adherent patients. These findings underline the impact of a simple strategy to combine a very effective and safe combination of statin + ezetimibe in a single formulation pill that would improve not only adherence but consequentially significantly reduce ASCVD events as well.


**Initiation of statins after carotid artery stenting**

In patients that needed a coronary stent procedure, statin therapy is a “conditio sine qua non.” The use of statins after the placement of carotid stenting lacks randomized placebo-
controlled trial evidence. This retrospective observational study in a single Chinese hospital re-evaluated the outcomes of patients that started with statins after their carotid stent placement vs. patients that did not initiate statin therapy. The authors selected 100 patients from their registry, 50 individuals the started a statin post-intervention, and 50 patients that did not. All patients had an indication for carotid artery stent (CAS) placement, aged 20 – 75 years old. The outcome endpoints were degree of neurological defect (as measured by the National Institute of Health Stroke Scale), lipid profiles (mg/dL), and CAS complications <30 days post-intervention. No differences were observed between the two groups for NIH Stroke Scale and mortality. Significant improvements were observed for total cholesterol (P=.03), LDL-c (P=.01), the risk for TIA (P=.03), ischemic stroke (P=.04), and cardiac complications (P=.03). These improvements were noted <30 days after the CAS procedure. These observational findings point toward the potential benefit of post CAS statin initiation for important cardiac and stroke outcomes. These findings do need to be confirmed in larger prospective studies to corroborate the suggested benefits.


Patients with diabetic nephropathy showed significant improvement in renal function with atorvastatin

The benefit of atorvastatin in patients with diabetic nephropathy was studied in a small group of Chinese diabetic patients diagnosed with diabetic nephropathy. Patients were randomly assigned to atorvastatin 20 mg or control and followed for three months. The authors evaluated rheological parameters (whole blood viscosity, erythrocyte aggregation index, and fibrinogen), renal function biomarkers (macrophage migration inhibitory factor (MIF), vascular cell adhesion molecule (VCAM)-1, Secreted frizzled-related protein-5 (SFRP5), and mAlb/Cr) and inflammatory markers (C-reactive protein (CRP), interleukin-1 (IL-1), and tumor necrosis factor-α (TNF-α)). Compared to the control group, blood viscosity, erythrocyte aggregation index, FIB, MIF, VACM-1, mAlb/Cr, CRP, IL-1, and TNF-α levels in the observation group significantly decreased. The levels of SERP-5 significantly increased (overall P<0.05). These findings show that atorvastatin could benefit patients with diabetic nephropathy by improving rheological parameters as well as renal function and inflammatory biomarkers.


Should aspirin be included in the fixed dose poly-pill?
The burden of CVD disease is increasing exponentially in developing economies; the impact on human suffering and the economic burden is unprecedented and will continue to grow exponentially if measures to improve risk factors causally associated with ASCVD are properly managed. The models used in developed economies are not applicable for the poorer regions of the world due to lack of infrastructure, trained staff, and costs for such sophisticated health care infrastructure. Alternative simple and low-cost approaches are needed to turn the tide of exploding ASCVD in not seldom relatively young patients. The polypill concept was developed to provide individuals at risk, based on age and sex, a cheap, safe, and effective solution to adequately lower blood pressure and LDL cholesterol. This meta-analysis combined the findings of three large poly pill studies (TIPS-3, HOPE-3, and PolyIran) that included 18 162 participants. The key question of this meta-analysis was if the addition of aspirin to a fixed-dose single pill formulation would improve outcomes or if this would increase bleeding complications. The primary outcome was the time to the first occurrence of a composite of cardiovascular death, myocardial infarction, stroke, or arterial revascularization. Secondary outcomes included individual cardiovascular outcomes and death from any cause. The estimated 10-year ASCVD risk was 17.7% (8.7). The median follow-up was 5 years. The primary was observed in 276 (3.0%) participants that used the polypill, compared with 445 (4.9%) in the control group; HR: 0.62 (0.53–0.73, p<0.0001). Myocardial infarction HR: 0.52 (0.38–0.70); revascularization HR: 0.549 (0.36–0.80), stroke HR: 0.59, (0.45–0.78), and cardiovascular death HR: 0.65 (0.52–0.81). Patients that used an aspirin-containing polypill showed greater reduction when compared to patients in whom aspirin was not part of their polypill. No differences were observed for different lipid, blood pressure levels and in the presence or absence of diabetes, obesity, or smoking. Bleeding complications in aspirin users were uncommon; GI bleeds in 19 (0.4%) in patients using aspirin vs. 11 (0.2%) in those that did not (p=0.15). Hemorrhagic stroke, fatal bleeding and peptic ulcer were rarely experienced; 10 (0.2%) vs 15 (0.3%), 2 (<0.1%) vs 4 (0.1%) and 32 (0.7%) vs 34 (0.8%), respectively. Using a fixed-dose combination polypill is an effective strategy to reduce fatal and non-fatal ASCVD events in primary prevention. Low costs and wide applicability make this an attractive and realistic approach to reducing the imminent ASCVD complications surge in developing economies.


Relevant publications


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**Basic Science publications**


4. Ren Y, Li L, Wang MM et al. Pravastatin attenuates sepsis-induced acute lung injury through decreasing pulmonary microvascular permeability via inhibition of Cav-


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