A retrospective cohort study on factors influencing the initiation of lipid-lowering therapy in hospitalized patients following a cardio-cerebrovascular event

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Introduction: Current European guidelines on cardiovascular prevention recommend lipid-lowering therapies for patients who have experienced an atherosclerotic cardiovascular disease (ASCVD) event.
Objectives: This study aims to provide updated data on the prescription of lipid-lowering therapies in patients discharged after an ASCVD event and to investigate the characteristics associated with a higher likelihood of receiving such therapy following the event.
Methods: Using administrative data from the Lombardy region, individuals of both sexes aged ≥40 years hospitalized for an incident ASCVD event during the first nine months of 2019 were identified. The prevalence of those receiving a prescription for lipid-lowering therapy within 90 days of the event was assessed. A multivariable logistic regression model was applied to evaluate the impact of various factors on the likelihood of initiating treatment (odds ratio [OR] and 95% confidence intervals [95%CI]).
Results: In a cohort of 18,370 individuals with an incident ASCVD event, 50.70% did not receive a prescription for any lipid-lowering therapy. The likelihood of initiating therapy was higher in individuals who experienced a cardiovascular event compared to a cerebrovascular event (OR 2.94, 95%CI 2.74-3.14), in patients aged 51-60 years (OR 1.22, 95%CI 1.10-1.36, compared to 61-70 years), and in those receiving antidiabetic (OR 1.42, 95%CI 1.25-1.61) or antihypertensive therapy (OR 1.77, 95%CI 1.64-1.92). Conversely, older age (71-80 years: OR 0.70, 95%CI 0.64-0.77; >80 years: OR 0.38, 95%CI 0.35-0.42), female sex (OR 0.81, 95%CI 0.75–0.87), prior exposure to antithrombotic medication (OR 0.67, 95%CI 0.60-0.73), and excessive polypharmacy (OR 0.57, 95%CI 0.49-0.66 for ≥10 medications) were associated with a lower likelihood of initiating treatment after the event.
Conclusions: The study highlights a suboptimal initiation of lipid-lowering therapy in patients discharged after an ASCVD event. Additionally, the results emphasize the importance of understanding influencing factors to improve patient management in secondary prevention.

Angiopoietin-like 3 (ANGPTL3) deficiency alters metabolic substrates utilization and reprograms hepatic metabolism

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Angiopoietin-like 3 (ANGPTL3) is a lipases-inhibiting hepatokine, thus prevents VLDL and LDL-derived triglycerides, regulating fluxes of triglycerides to the tissues. Aim of this study is to investigate the association between hypolipidemia-induced metabolic alteration, due to ANGPTL3 deficiency, and potential hepatic responses, depending on the source of energetic substrates available.
Full-knockout (KO) mice and littermate controls (WT) underwent a standard chow diet or High Fat Diet (HFD, 60% kcal from fat) regimen for 16 weeks. Metabolic responses have been assessed through indirect calorimetry, lipid, glucose and insulin tolerance test, and circulating lipid levels have been evaluated.
ANGPTL3 KO mice are hypolipidemic at fasting, postprandially and in fast refeeding, both at chow and HFD.
After an oil gavage, ANGPTL3 KO mice absorb less triglycerides both at fasting (area under curve: HO:3320.8mg/dL*min±1214.9vsWT:17303 mg/dL*min±11765.2, p=0.07) and postprandially (area under curve: HO:447.3mg/dL*hr±20.9vsWT: 938.2mg/dL*hr ±294.9, p=0.016), and this associates with a lesser hepatic lipoprotein production, also at HFD. Glucose metabolism is not affected, and liver histology of KO mice at chow and HFD do not show increased steatosis compared to control group. Indirect calorimetry data show an increased trend of oxidative metabolism in the postprandial phase compared to controls (Respiratory Exchange Ratio at ZeitgeberTime21: HO: 0.889±0.102vsWT: 0.969±0.089; p=0.074).
Hepatic mTOR activation has been investigated with western blotting, to understand a possible nutrient sensing alteration, by evaluating the phosphorylation of downstream effectors S6K (fold on housekeeping: HO:0.28±0.122vsWT:0.647±0.119; p=0.021) and 4E-BP1 (fold on housekeeping: HO: 0.503±0.193vsWT:1.043±0.270, p=0.048) and a dampened activation is observed. This is associated with a lower protein synthesis. RNA sequencing data confirmed that at chow diet KO mice face the activation of metabolic pathways such as urea cycle and bile acids production. Hepatic signalling pathways, like LXR, are blunted, at chow and HFD.
ANGPTL3 deficiency alters the metabolic phenotype, reducing circulating lipemia, and an adaptive metabolic response occurs depending on the metabolic substrate availability.