that medical therapy fails to ameliorate this. This may be due to side effects and limited efficacy of medications at tolerable doses. **Methods:** We conducted a retrospective study on 201 patients with PA treated with medical therapy (spironolactone, eplerenone or amiloride) for PA from 2000–2020 at two tertiary centres. Patients were assessed for efficacy to achieve clinical and biochemical control, and for side effects. **Results:** 53.7% of patients achieved blood pressure <140/90mmHg, 44.6% achieved serum potassium ≥4.3mmol/L, and 63.2% achieved renin levels >1ng/ml/hr. Concordance between biochemical control as assessed by potassium and renin levels was 49%. 45.3% of patients experienced side effects, with 8.5% switching to another medication, 18.9% decreasing dose, and 10.0% stopping medications altogether. Risk factors for side effects were spironolactone use, dose ≥50mg, duration of treatment ≥1 year, male gender and unilateral PA. Patients with unilateral PA, compared to bilateral PA, used higher median doses of spironolactone, 75mg vs 50mg, P<0.001, but more had persistent hypokalemia, 20.5% versus 6.4%, P=0.007. 44 patients with unilateral PA underwent surgery after initial medical therapy, which further improved systolic and diastolic BP, from 142 to 134mmHg, P<0.001, and from 85 to 79mmHg, P<0.001, respectively. **Conclusion:** Dose-dependent side effects limit the efficacy of medical therapy in PA. Future prospective studies should assess the best monitoring strategy for biochemical control during long-term medical therapy. In patients with unilateral PA, surgery remains a better option compared to life-long medications.

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Total Testosterone Confounds the Association Between Total Bilirubin and Dyslipidemia

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Background: The mechanism for the association between total bilirubin (TBili) and dyslipidemia remains unclear. Total testosterone (TT) has been implicated in reducing bilirubin conjugation and decreasing atherogenic lipids. We hypothesized that 1) TBili was inversely associated with dyslipidemia, and 2) TT confounded this association.
Methods: Our study population consisted of 5,878 (2,730 male and 3,148 non-pregnant female) adults aged ≥20 years from the 2011–2016 National Health and Nutrition Examination Survey (NHANES). We excluded those taking self-reported cholesterol medications. Participants with transaminitis (AST or ALT >45 IU/L; AST/ALT >5), excessive alcohol consumption (>20 drinks/week for males; >10 for females), iron overload (transferrin >50%), or positive hepatitis B/C serology were also excluded. We categorized TBili into sex-specific quartiles (Male: <0.5, 0.5–0.6, 0.6–0.8, ≥0.8 mg/dl; Female: <0.4, 0.4–0.5, 0.5–0.6, ≥0.6). Dyslipidemia was defined as elevated TG (≥150 mg/dl) or low HDL (<40 mg/dl for male; <50 for female). We used survey design-adapted multivariable logistic regression, adjusting for TT, demographics, cardiometabolic factors, and liver function. We also stratified by sex-specific median TT levels (386 ng/dl in males; 18.5 ng/dl in females) to determine effect modification. Further, we determined whether the association between TBili and dyslipidemia persisted in males with TT deficiency (<280 ng/dl).
Results: Among the 5,878 adults, 1,013 (38%) males & 958 (30%) females had elevated TG, and 803 (29%) males & 1,146 (33%) females had low HDL. Males in the highest quartile (Q4) of TBili had age-adjusted, mean (SD) 50.1 (3.5) mg/dl lower TG and 4.0 (0.9) mg/dl higher HDL than males in the lowest quartile (Q1; p<0.0001). Females in Q4 had 36.4 (4.9) mg/dl lower TG and 5.1 (1.4) mg/dl higher HDL than Q1 (p<0.0001). Males and females in Q4 had 60% and 59% lower odds, respectively, of elevated TG compared to Q1 (adjusted OR [95% CI]; Male: 0.40 [0.28, 0.57], Female: 0.41 [0.32, 0.52]). Males and females in Q4 had 44% and 39% lower odds, respectively, of low HDL compared to Q1 (Male: 0.56 [0.38, 0.81], Female: 0.61 [0.42, 0.90]). Adjusting for TT increased the parameter estimate for Q4, relative to the univariate estimate, by 21% in both sexes. There was no significant difference in TT-stratified odds of elevated TG or low HDL. Among the 544 (19%) males with TT deficiency, Q4 had 56% lower odds of elevated TG and 46% lower, but insignificant, odds of low HDL (aOR [95% CI]; TG: 0.44 [0.21, 0.89], HDL: 0.54 [0.26, 1.12]).
Conclusion: TBili was inversely associated with elevated TG and low HDL. TT confounded, but did not modify, this association. Future studies examining TBili's antiatherogenic role should adjust for TT.

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Trends in Serum Lipid Profiles and Lifestyle Factors Among Korean Adolescents, 2007–2018

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Objectives: Trends in serum lipids among teenagers would be crucial predictors of potential cardiovascular disease in adults. We aimed to investigate the trends in lipid profiles and related factors, including obesity, smoking, exercise, alcohol use, and total fat intakes in Korean adolescents from 2007 to 2018. **Methods:** We analyzed 5,967 participants aged 12–19 yrs from the Korea NHANES 2007–2018. Fasting total cholesterol, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), and triglycerides (TG) levels were measured. **Results:** All kinds of lipid profiles, except TG, showed increasing trends from 2007 to 2018 (P<0.01). Nevertheless, the prevalence of dyslipidemia showed a trend of decreasing in boys (from 33.3 to 26.6%; P=0.002) and maintained in girls (from 28.4 to 30.2%; P=0.465), mainly due to a substantial decrease in hypo-HDL-cholesterolemia (9% reduction in boys, 5% reduction in girls). This occurred amid an increasing trend of central obesity in boys (P<0.001). In lifestyle factors, there

were no significant changes in alcohol use and muscle-strengthening exercise, while a substantial decrease in smoking rate was observed. A favorable effect of muscle-strengthening exercise on both TG and HDL-C and an unfavorable impact of smoking on HDL-C were observed. Alcohol use was associated with higher HDL-C in both genders, but it showed opposite associations with TG between boys (unfavorable) and girls (favorable). Regarding dietary factors, there were increasing trends in total fat intakes and the percentage of energy supply from total dietary fat (〔total fat (%E)〕 in both genders. In boys, an increase in total fat (%E) was related to the higher HDL-C in normal-weight subjects (P<0.01 in both genders); however, it was associated with higher LDL-C in overweight girls (P=0.001). **Conclusions:** Increases in fat intakes and a decline in smoking rates appeared to have positively impacted HDL-C in Korean adolescents over the past 12 years. We confirmed a rise in fat intakes was linked with the increase in LDL-C among overweight adolescents. Therefore, close monitoring for the dyslipidemia prevalence is essential in Korean adolescents whose obesity prevalence is on the rise.

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ULK1 Regulates Hepatic Lipid Metabolism via Autophagy Independent Mechanisms

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Non-alcoholic steatohepatitis (NASH), a major complication of obesity, diabetes, and metabolic syndrome has emerged as a leading cause of chronic liver disease and a risk factor for hepatocellular carcinoma. Autophagy is a critical pathway for the degradation of intracellular components by lysosomes. Established functions for autophagy in hepatic lipid metabolism and insulin sensitivity suggest a mechanistic link between altered autophagy and NASH. However, the interactions between insulin sensitivity, NASH, and autophagy are incompletely understood. The Unc-51 Like Autophagy Activating Kinase 1 (ULK1) is the only serine/threonine kinase in the core autophagy pathway and thus represents an excellent drug target. In this study, we observed that ULK1 may directly regulate insulin signaling and lipid metabolism via mechanisms that might involve modulation of AKT dephosphorylation. Surprisingly, silencing ULK1 did not significantly alter autophagy in hepatocytes despite impairing insulin-stimulated activation of AKT. To further elucidate the autophagy-independent role of ULK1 in hepatic lipid metabolism and insulin action, ULK1 liver-specific knock-out mice were generated. L-ULK1 KO mice exhibited impaired glucose tolerance and insulin resistance on a normal chow diet or 60% high-fat diet (HFD). In young mice (4 weeks after birth), the expression of genes that regulate de novo lipogenesis, such as FAS, SCD1, and SREBP1-c were induced in livers of L-ULK1KO mice even prior to the development of insulin resistance and obesity. Hepatomegaly and lipid accumulation developed in L-ULK1KO on normal chow and was exacerbated relative to wild type mice on a HFD. Serum concentrations of insulin, triglyceride, cholesterol, AST and ALT were significantly increased. In contrast, L-ULK2 KO mice were phenotypically normal. To identify putative novel ULK1 targets, we conducted a phospho-proteomics screen in a ULK1 deficient hepatocyte cell line. We identified a relatively small number of novel proteins whose phosphorylation levels were reduced by ULK1 deficiency. The identification of these targets supports autophagy-independent mechanisms of action of ULK1. Recently, we confirmed that NCOA3, one of the targets regulates hepatic lipid metabolism by interacting directly with ULK1. These data suggest that ULK-1 may regulate cellular targets that regulate hepatic lipid metabolism and insulin sensitivity.

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Utility of Plasma Metanephrines in Adrenal Venous Sampling in Primary Aldosteronism

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Introduction: Adrenal Venous Sampling (AVS) is the most reliable means of identifying surgically curable subtypes of primary aldosteronism (PA). Cortisol levels are used to determine cannulation success and lateralization. However, cortisol has a variable secretion pattern and long-half life, and can be co-secreted by adrenal adenomas, leading to misinterpretation of results. Plasma metanephrines (MN) are a possible alternative analyte. MN levels are unaffected by stress, have a short half-life of 3–6 minutes and are released continuously by the adrenals, resulting in very high concentration gradients between the adrenal veins (AV) and peripheral veins (PV), thus providing a sensitive means to determine cannulation success. *Premise:*The objective of this study was to see if MN can be used in lieu of cortisol in AVS. A secondary end-point was to see if the data was particularly useful in patients who are known co-secretors of cortisol. **Methods:** Data from AVS carried out without cosyntropin stimulation, from October 2018 to March 2020, were analysed retrospectively. Of these, 51 had additional samples drawn for MN at the time of the procedure and were recruited. Six patients were identified as having autonomous cortisol secretion as they failed an overnight dexamethasone suppression test (ONDST). The data was analysed using cortisol and MN separately and then compared with regards to their selectivity and lateralization index. Data was also analysed to see if known co-secretors had an elevated cortisol/MN ratio of more than 2 on the affected side as described in previous papers. **Results:** When compared to cannulation and lateralization outcomes using cortisol, similar results were obtained using, a MN AV/PV ratio of more than 12 to indicate successful cannulation and an aldosterone/MN ratios of greater than 5 to confirm lateralization. Contralateral suppression