Guided Poster Presentation 2

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GPP 2-1 5. Diabetes and Obesity

T-cell receptor repertoire profiles in peripheral blood and adipose tissue of patients with severe obesity with and without type 2 diabetes mellitus

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Background: Severe obesity without metabolic alterations (Metabolically Healthy Obesity, MHO) is associated with a lower risk of death and cardiovascular disease compared to severe obesity with metabolic alterations (Metabolically Unhealthy Obesity, MUO). Inflammation is considered as the key risk factor in mediating the metabolic dysfunction in obesity. The dysregulation of T cell immune homeostasis in blood and adipose tissue in patients with severe obesity in relation to chronic inflammation is well acknowledged. However, the characteristics of T-cell receptors (TCR) repertoire in MHO and MUO remain largely unexplored.

Methods: High-throughput sequencing of TCR repertoires was conducted on peripheral blood and adipose CD4+ T cells from subjects with MHO (n = 3; age = 33.6 ± 11 years; BMI = 35.9 ± 4.7; HbA1c = 5.2 ± 0.2) and subjects with severe obesity with type 2 diabetes mellitus (T2DM) representing the MUO group (n = 4; age = 32.7 ± 9 years; BMI = 35.0 ± 1.6; HbA1c =10.1± 1.5).

Results: Analysis of TCR repertoires in peripheral blood samples showed that the number and diversity of V-J combinations in the MUO group tended to be more skewed compared to that of the MHO group. The usages of the V gene and V-J pair, along with the frequency distributions of some complementarity-determining region 3 (CDR3) amino acids (AAs) in TCR differed significantly between the two groups. Unique TCR CDR3 clonotypes were mildly decreased in the MUO subjects. A higher similarity of TCR V-J distribution and an increased frequency of differentially expressed V-J gene segments with shorter CDR3 length were identified in the MUO group. Profiling of TCR repertoire in adipose tissue CD4+ T cells also showed significantly shorter CDR3 lengths and a higher frequency of several variable genes including TRBV12–4, TRBV18, TRBV7-9 in the MUO group compared to that of the MHO group.

Conclusion: This study demonstrates potential variations and unique properties of TCR repertoires in peripheral blood and visceral adipose tissue in patients with severe obesity with and without T2DM. These findings could guide the development of potential biomarkers to distinguish MHO and MUO and inform future immunotherapeutic strategies for patients with severe obesity with T2DM.

GPP 2-2 7. Other Comorbidities of Obesity and Metabolic Syndrome

Effectiveness of GLP1-RA as a Therapy for NAFLD in Type 2 Diabetes: A Systematic Review

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Background: One of the most common complications of type 2 diabetes mellitus (T2DM) is non-alcoholic fatty liver disease (NAFLD), which occurs due to insulin resistance, obesity, and inflammation. These two diseases exacerbate each other, increasing mortality in T2DM patients. However, current NAFLD therapies are limited to lifestyle improvements, prompting extensive research into glucagon-like peptide 1 receptor agonists (GLP1-RA) as a potential anti-diabetic drug that can improve liver function. This study aims to demonstrate the effectiveness of GLP1-RA in improving liver enzymes (AST, ALT, and GGT) in T2DM patients with NAFLD.

Methods: A systematic literature search was conducted through PubMed, ProQuest, EBSCOhost, and ScienceDirect. Inclusion criteria encompassed studies from the last five years that investigated the effects of GLP1-RA on T2DM patients with NAFLD. The quality of the studies was assessed using the CEBM Oxford criteria for therapeutic studies.

Results: Out of 257 studies, nine high-quality studies (N=298) met the inclusion criteria. All studies indicated that GLP1-RA administration successfully reduced AST and ALT levels, with 5 studies showing significant reductions ($p<0.05$). AST levels decreased by 3-33.4 U/L, while ALT levels decreased by 5.9-40.1 U/L. Seven of the 9 studies reported GGT reductions of 1-32.9 U/L, with 4 studies showing significant decreases. The most frequently used GLP1-RA drug was liraglutide, with a significant impact observed at 24 weeks of administration.

Conclusion: GLP1-RA has been proven to reduce inflammation by lowering liver enzyme levels of AST, ALT, and GGT, making it an effective therapeutic option for T2DM patients with NAFLD. Future research on the impact of GLP1-RA on liver biopsy or elastography outcomes could further support these findings.

GPP 2-3 2. Nutrition, Education and Exercise for Obesity

Regulation of Ferroptosis in Obesity: Muscle Type-Specific Effects of Dietary Restriction and Exercise

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Background: Obesity is a significant global health issue and a risk factor for numerous diseases. Ferroptosis, an iron-dependent regulated cell death, is triggered by iron overload and the excessive accumulation of lipid peroxidation mediated by reactive oxygen species. Recent research has identified a strong association between ferroptosis and obesity. Additionally, dietary restriction (DR) and DR combined with exercise (DR+Ex) are effective strategies for managing obesity and ferroptosis. However, the regulation of ferroptosis and its signaling pathways in skeletal muscle under conditions of obesity, DR, and DR+Ex remains poorly understood.

Methods: Mice were divided into four groups: normal diet, high-fat diet, 20% high-fat DR, and 20% high-fat DR+Ex. All mice were fed ad libitum with either a normal or high-fat diet for the first 14 weeks, followed by normal diet, high-fat diet, 20% high-fat DR and 20% high-fat DR+Ex for the last 8 weeks, separately. The left gastrocnemius muscle was examined for ferroptosis using immunohistochemistry, H&E, Masson's trichrome, and Prussian blue staining. Muscle type-specific expression of ferroptosis signaling proteins in the right gastrocnemius muscle was analyzed by Western-Immunoblot.

Results: The high-fat diet resulted in significantly increased inflammatory cell infiltration, fibrosis, and iron accumulation in skeletal muscle ($P < .05$). Additionally, red and white muscles showed increased expression of 4-HNE, regulated by GPX4 and NCAO4, respectively ($P < .05$). Although high-fat DR and DR+Ex did not significantly impact fibrosis and iron accumulation in skeletal muscle ($P > .05$), they reduced downstream 4-HNE expression by regulating GPX4 in red muscle ($P < .05$).

Conclusion: Red and white muscles respond to obesity-induced ferroptosis through different signaling pathways. The regulation of ferroptosis by DR and DR+Ex is muscle type-specific. Specifically, red muscle is more sensitive to the regulation of ferroptosis signaling by DR and DR+Ex compared to white muscle..

GPP 2-4 11. Obesity and Metabolic Syndrome in Children and Adolescents

Exploring Pediatric Health: Unraveling Obesity Prevalence and Activity Patterns in East Asia

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Background: Pediatric obesity is a global health concern, also in the East Asia. Physical inactivity is a risk factor for pediatric obesity. Physical activity is important to maintain and improve health, yet disparities persist across different regions. This study endeavors to explore the variations in physical activity levels and the prevalence of pediatric obesity across Korea, China, and Japan.

Methods: Analyzing data sourced from the NCD Risk Factor Collaboration, our study scrutinized the trends in overweight including obesity prevalence among children and adolescents across Korea, Japan, and China, from 2013 to 2022. Obesity and overweight were defined as a BMI of more than 2 SD and 1 SD above the median of the WHO growth reference. Additionally, as part of global initiatives led by the Active Healthy Kids Global Alliance, we compared and analyzed key data and international indicators of physical activity released in the Global Matrix to assess changes in physical activity.

Results: Korea showed higher prevalence than China and Japan, especially in boys. The regression equations for predicting BMI based on gender are calculated by country. The trends in physical activity and related factors from 2018 to 2022 show varying levels of change. Korea experienced a no change in overall physical activity, while sedentary behavior improved slightly, and governmental policies showed notable enhancement. China showed improving levels of physical activity, with no notable changes in governmental policies. Japan exhibited improvements in physical fitness, active transportation, community and environment, with stable levels of sedentary behavior and moderate governmental policies throughout the period.

Conclusion: Understanding the patterns of physical activity is essential for crafting precise interventions and policy frameworks for fostering active lifestyles. We emphasize the importance of reassessing strategies for managing increasing pediatric obesity in Korea, despite the presence of improving governmental policies, indicating a need for targeted interventions.

GPP 2-5 7. Other Comorbidities of Obesity and Metabolic Syndrome

Relationship between obstructive sleep apnea and cardiovascular health in middle-aged Korean men and women: a nationwide study

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Background: Cardiovascular health (CVH) can be conceptualized as encompassing 7 health behaviors and metabolic factors that contribute to cardiovascular disease. We explored the relationship between the risk of obstructive sleep apnea (OSA) and CVH among middle-aged Korean adults.

Methods: Data from 5909 participants in the Korea National Health and Nutrition Examination Survey (2019–2021) were analyzed. The risk of OSA was assessed using the STOP-Bang questionnaire, with score of 0–2, 3–4, and 5–8 indicating low, moderate, and high risk, respectively. CVH metrics, including smoking status, diet, physical activity, body mass index (BMI), blood pressure, total cholesterol level, and fasting glucose concentration, were evaluated using American Heart Association criteria. Each metric was assigned a score of 2 (ideal), 1 (intermediate), or 0 (poor). The sum of these scores was used to assess overall CVH. A total score of ≥12 was classified as ideal, 8–11 as intermediate, and ≤7 as poor CVH. Multivariate logistic regression analysis was employed to investigate the association between OSA risk and CVH.

Results: Among study participants, 78.6% of men and 16.3% of women displayed moderate-to-high risk of OSA, while 45.4% of men and 17.2% of women exhibited poor CVH. In the multivariate model, the odds ratios (95% confidence intervals) for poor CVH were 2.69 (2.08–3.49) for men at moderate risk of OSA and 6.54 (4.81–8.90) for those at high risk, compared to men at low risk. For women, the odds ratios were 3.21 (2.47–4.19) for those with moderate risk and 12.88 (6.29–26.38) for those with high risk of OSA, compared to women at low risk. CVH metrics associated with moderate-to-high OSA risk included high BMI, high blood pressure, elevated fasting glucose, and smoking.

Conclusion: The risk of OSA was associated with poor CVH, while various CVH components were linked to moderate-to-high OSA risk. Therefore, managing both OSA and components of CVH is essential to minimize poor CVH.

GPP 2-6 5. Diabetes and Obesity

Long-term weight loss in the SELECT trial: semaglutide 2.4 mg vs placebo over 208 weeks in a global population of 17,604 participants

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Background: The SELECT cardiovascular (CV) outcome trial provided the opportunity to study weight and anthropometric effects of semaglutide vs placebo over 4 years of intervention in a large, geographically and racially diverse population of individuals with body mass index (BMI) ≥27 kg/m2 and pre-existing CV disease, without type 2 diabetes.

Methods: SELECT, a multicentre, randomised, double-blind, placebo-controlled, event-driven superiority trial, enrolled 17,604 patients aged ≥45 years. Patients were randomly assigned to receive once-weekly subcutaneous semaglutide 2.4 mg or placebo in addition to standard of care recommendations for secondary prevention of CV disease, including healthy lifestyle counselling without specific weight-loss instruction. This prespecified, as-treated analysis examined the effect of semaglutide and placebo on weight change, anthropometric measures and subgroups based on baseline demographics, weight-related and glycaemic measures. We assessed the following measures: change in body weight (%); change in waist circumference (WC, cm); change in WC/height ratio (WHtR) and change in BMI category.

Results: With semaglutide, weight loss continued to week 65 and then weight was sustained for the rest of the study. Mean percent weight losses with semaglutide 2.4 mg vs placebo at years 2, 3 and 4 are shown (Figure 1A). At 208 weeks, semaglutide was associated with robust and sustained weight loss (average −10.18%), reduced WC (average −7.73 cm) and improvement in average WHtR (−6.85%) as compared with placebo at the same time points (−1.53%, −1.34 cm and −0.99%, respectively; p<0.0001 for all comparisons vs placebo). These improvements were seen across both sexes and all categories of race, age, baseline glycaemic status and degree of adiposity. We analysed change in BMI category at week 104 (Figure 1B). More patients in the semaglutide-treated group (52.4%) experienced improvement in BMI category compared with those receiving placebo (15.7%). In the semaglutide group, 12% reached a BMI <25 kg/m2 compared with 1.2% for placebo.

Conclusion: In SELECT, use of once-weekly subcutaneous semaglutide 2.4 mg produced clinically significant and durable weight loss and improvements in anthropometric measurements over 4 years in individuals with BMI >27 kg/m2 and pre-existing CV disease from diverse racial and geographic backgrounds and with varied body anthropometrics.