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AACE
ANNUAL MEETING
May 12-14, 2022

AMERICAN ASSOCIATION OF CLINICAL ENDOCRINOLOGY

ANNUAL MEETING 2022

DAILY COVERAGE

TOP 7 SESSIONS: DAY-1

TOPIC OF CONTENT

SESSION-1: OPTIMIZING INSULIN THERAPY-STORIES FROM AROUND THE WORLD SPONSORED BY MEDTRONIC

INSULIN FOR HYPOGLYCEMIA? THE CASE FOR INITIATING PRANDIAL INSULIN FIRST IN CYSTIC FIBROSIS RELATED DIABETES

Thursday, 12th May 2022

This paper was presented on May 12th at the 30th Annual Meeting of the American Association of Clinical Endocrinology (AACE) at San Diego, by Dr. Barbara Simon MD from the Thomas Jefferson University Hospital.

Cystic fibrosis related diabetes (CFRD) is the most common non-respiratory comorbidity in cystic fibrosis (CF), occurring in 40-50% of adults with CF. CF mediated destruction of the pancreatic tissue from progressive fibrosis and fatty infiltration leads to loss of beta cells and insulin deficiency, but alteration of beta cell function and insulin resistance due to inflammation or infection are also possible mechanisms for diabetes development.

"This case describes an 18-year-old female who was diagnosed with CF in infancy and presented to our clinic for evaluation of possible CF related diabetes and hypoglycemia. Lab tests 4 months earlier revealed a HgbA1c of 5.7, oral glucose tolerance testing (OGTT) showed a fasting blood glucose level of 87 mg/dL, 246 mg/dL one hour and 222 mg/dL two hours after glucose load. She reported that after large meals- especially those that were carbohydrate rich- she felt sweaty, anxious, and weak. Her initial CGM tracing revealed marked post-prandial hyperglycemia above 250 mg/dL followed by precipitous drops to 70 mg/dL or less. We chose to initiate our patient on a bolus only regimen (rapid acting insulin prior to meals) which resulted in less post-prandial hyperglycemia and resolution of her hypoglycemic episodes." explained Dr. Simon.

The patient's elevated OGTT with normal fasting glucose are consistent with the diagnosis of CFRD without FH (fasting hyperglycemia). Insulin use in CFRD patients is associated with better lung function, improvement in nutritional status, and reduction in pulmonary complications. Traditional management of CFRD starts with daily basal insulin, and published clinical care guidelines suggest CFRD with FH be started on basal or basal-bolus insulin regimens, but guidelines for patients without FH are less clear. One study showed benefits of prandial insulin in reversing weight loss, but more research is needed. An additional concern in our case was post prandial hypoglycemia. This hypoglycemia in CF patients is likely due to impaired early insulin secretion with delayed and possibly compensatory increase in late insulin release, as well as diminished glucagon secretion in the setting of alpha cell failure. "In this case, prandial insulin not only treated her hyperglycemia, but also- paradoxically- prevented her hypoglycemia.

Although there is a lack of research around initiating bolus only insulin regimens for CFRD, we believe that this is an important and appropriate first line treatment for many patients with CFRD without FH, and for prevention of hypoglycemia due to delayed and dysregulated endogenous insulin secretion."

A THERAPEUTIC PARADOX: USING INSULIN TO TREAT GASTRIC BYPASS ASSOCIATED HYPERINSULINEMIC HYPOGLYCEMIA

Thursday, 12th May 2022

This paper was presented on May 12th at the 30th Annual Meeting of the American Association

of Clinical Endocrinology (AACE) at San Diego, by Drs Bianshly Rivera Rivero, MD Joshua Rosenwasser, MD Natalia Weare-Regales, MD, Carlos Palacio, MD Omar Santana Hernández, MD from the University of Florida.

Hyperinsulinemic hypoglycemia is an uncommon complication of gastric bypass surgery. Diagnosis of this condition and optimal treatment remains a challenge. We present a case of gastric bypass-associated hyperinsulinemic hypoglycemia successfully treated with insulin.

A 40-year-old female with a medical history of undifferentiated connective tissue disease, schizoaffective disorder, fibromyalgia, Raynaud's phenomenon, pulmonary embolism, and morbid obesity status post gastric sleeve and a revision to Roux-en-Y gastric bypass was evaluated for recurrent postprandial hypoglycemia occurring about 1-2 hours post meals. The symptoms developed one year after gastric bypass. She initially had neuroglycopenic symptoms but now had hypoglycemia unawareness with several hypoglycemic emergencies requiring Emergency Medical Service intervention that necessitated her getting a Continuous Glucose Monitor. The lowest sugar on record was 27 mg/dl on self-monitoring blood glucose. Initial symptoms of hypoglycemia and hypoglycemia would resolve upon administration of glucose. There was no fasting or nocturnal hypoglycemia and eating lower carbohydrate meals helped. She was offered a biochemical evaluation for hypoglycemia but was unwilling to do a fasting or mealtime study. Abdominal imaging did not reveal pancreatic masses. Based on the clinical presentation, a diagnosis of post gastric bypass hyperinsulinemic hypoglycemia was suspected.

She received nutritional counseling on eating low, complex carb, and frequent meals. Multiple medications were tried without success that included Acarbose, Octreotide, Diazoxide, and Metformin. The patient was then started on Aspart insulin 1 unit per 25 grams of carbohydrates before meals with the goal of decreasing the postprandial glycemic spike that would ultimately lead to hypoglycemia. This caused a marked reduction of postprandial hypoglycemic events and no further hypoglycemic emergencies were reported.

"We present a novel non-invasive and cost-effective option for treating hyperinsulinemic hypoglycemia after gastric bypass surgery. The use of insulin therapy before meals targeted to avoid a postprandial spike reduced the incidence of postprandial hypoglycemia by reducing the stimulus on endogenous pancreatic insulin release." Said Dr. Rivero.

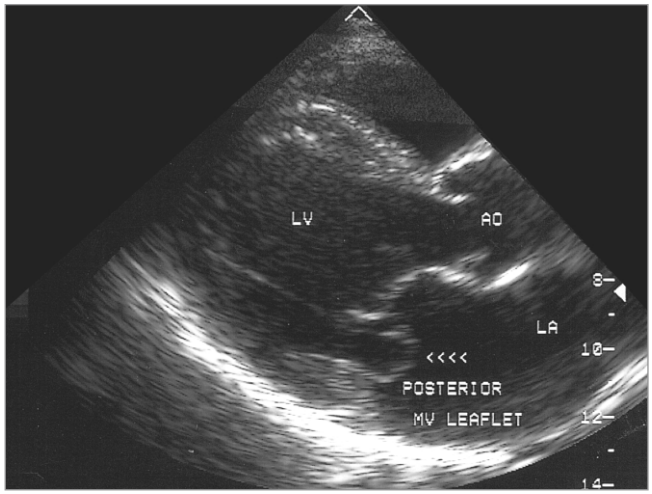
SESSION-2: THE EVALUATION AND MANAGEMENT OF HYPERTHYROIDISM IN PREGNANCY

MITRAL VALVE CHORD RUPTURE IN A PREGNANT PATIENT WITH UNCONTROLLED HYPERTHYROIDISM: A UNIQUE CASE

Thursday, 12th May 2022

This paper was presented on May 12th at the 30th Annual Meeting of the American Association of Clinical Endocrinology (AACE) at San Diego, by Drs. Nissa Blocher, MD, FACE Catherine Anastasopoulou, MD, FACE from the Einstein Medical Center, Philadelphia.

Hyperthyroidism can have vital clinical consequence regarding the cardiovascular system. "We present a very unusual case of a cardiac complication precipitated by both the hemodynamic changes of uncontrolled hyperthyroidism and pregnancy."



The patient is a 36-year-old female at 13 weeks gestation with uncontrolled Graves' disease recently started on propylthiouracil. She presented to the hospital with progressive shortness of breath, orthopnea, leg swelling, and palpitations. On presentation she was hemodynamically stable but tachycardic. EKG showed atrial flutter with variable A-V block. Laboratory studies were significant for a suppressed TSH of < 0.01 mcIU/mL (ref 0.35-4.94) and an elevated free T4 of 2.42 ng/dL (ref 0.70-1.48). A 2D echocardiogram showed eccentric moderate mitral regurgitation. Right heart catherization demonstrated elevated right and left filling pressures, mildly elevated pulmonary pressures with venous congestion. Given the severity of the mitral regurgitation, a transesophageal echocardiogram was done revealing severe mitral regurgitation with a ruptured chord and a markedly thickened, highly mobile chord. She was treated conservatively with IV diuresis and counseled about her high-risk pregnancy. She was followed as an outpatient by cardiology and endocrinology and switched to methimazole in her second trimester. She was readmitted secondary to preterm premature rupture of membranes at 23 weeks gestation and after a prolonged hospitalization delivered her baby at 28 weeks without major complication. She is pending a decision for definitive treatment for her Graves' disease.

There is an association between mitral valve prolapse and hyperthyroidism. Myxomatous degeneration of the valve leaflets causes thickening as well as tissue that can rupture with little stress. In pregnancy, cardiac output increases by around 30%, and there is a reduction in systemic vascular resistance. This is similar to the hemodynamics of uncontrolled hyperthyroidism whereby there is elevated preload, increased heart rate and cardiac output, and reduced systemic vascular resistance. Myxomatous degeneration of the mitral valve combined with the hemodynamic changes of uncontrolled hyperthyroidism and pregnancy, together likely precipitated the chord rupture in this patient. There have been cases described of chord rupturing occurring in context of hyperthyroidism, but this is the first case, to our knowledge to describe mitral valve chord rupture in context of both pregnancy and uncontrolled hyperthyroidism.

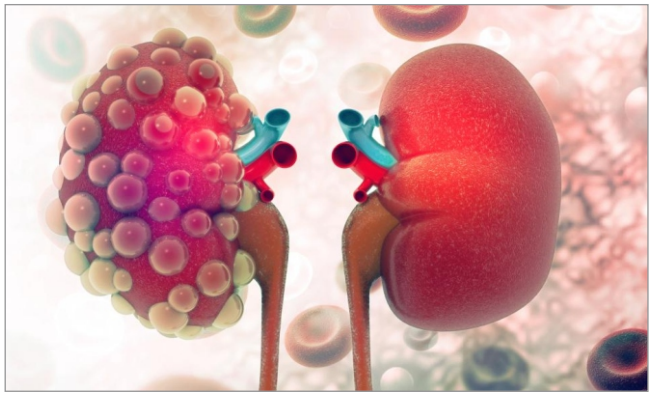
SESSION-3: WHAT'S NEW IN THE MANAGEMENT OF THE DIABETIC KIDNEY? A PRO/CON DEBATE

POOR OUTCOMES OF HOSPITALIZED COVID-19 PATIENTS WITH TYPE 2 DIABETES AND CHRONIC KIDNEY DISEASE

Thursday, 12th May 2022

This paper was presented on May 12th at the 30th Annual Meeting of the American Association of Clinical Endocrinology (AACE) at San Diego, by Drs. Vicky Cheng Debra Ella Burguera-Couce Geetha Gopalakrishnan Filipe Monteiro from the Warren Alpert Medical School of Brown University.

"Our objective was to evaluate the impact of CKD stages on health outcomes in hospitalized patients with T2D and COVID-19."



Data from 1122 patients with T2D admitted in Rhode Island with COVID-19 infection during the first wave (March 1 - June 30, 2020) and second wave (July 1, 2020 - February 28, 2021) were analyzed. Multivariate logistic regression analysis was conducted in SAS software to compare CKD stages (Stage 1/2/3a: GFR >45 mL/min, Stage 3b: GFR 30-44 mL/min, Stage 4: GFR 15-29 mL/min, Stage 5: GFR < 15 mL/min or dialysis) and severe COVID-19 by length of stay (LOS) ≥ 1 week, ICU admission, mechanical ventilation (MV), in–hospital mortality and readmission rates. The analysis was adjusted for age, race/ethnicity, gender, insurance status and admission month. Model to look for risk factors associated with poor outcomes (combined risk of ICU admission, MV and in-hospital mortality) was controlled for age, race/ethnicity, gender, insurance status, body mass index (BMI), hypertension (HTN), pulmonary disease, hyperglycemia, LOS and admission month.

In our cohort, patient with CKD stages 1/2/3a, 3b/4, 5 represented 50.4%, 35.1% and 14.4%, respectively. The mean (± SD) age was 70.4 ± 13.6 with 52% Male, 56% White/Caucasian, 23% Hispanic/Latino and 2% Black. HTN (88%), pulmonary disease (38%) and obesity (50%) noted. T2D patients with CKD stages 3b, 4, or 5 had longer LOS (OR 1.5 [1.1-2.1], 28.7 [10.5-78.2] respectively), higher likelihood of ICU admissions (OR 1.9 [1.2-3.0], 3.3 [2.1-5.2], 4.6 [3.0-7.1] respectively) and were more likely to die during hospitalization (OR 2.0 [1.1-3.6], OR 4.9 [2.8-8.5], OR 8.3[4.8-14.3] respectively). Adjusted model identified CKD stage 5 (OR 0.2 [0.04-0.6]), hyperglycemia (OR 8.9 [2.6-30.4]) and admission during the first wave (OR 2.3 [1.1-4.9]) to be independent risk factors for poor outcomes in hospitalized patients with T2D and COVID-19 infection.

To our knowledge, this is the first study to look at the impact of stages of CKD on the morbidity and mortality of T2D patients hospitalized with COVID-19 infection. Our study showed that hospitalized patients with T2D and CKD (GFR< 45 mL/min) are more likely to be admitted to the ICU, have longer hospital stays and potentially die as a result of their illness. Furthermore, CKD stage 5, hyperglycemia and hospital admission during the first wave were identified to be independent risk factor for poor outcomes in hospitalized patients with T2D and COVID infection.

SESSION-4: 2022 AACE FATTY LIVER GUIDELINE

AACE 2022: THE MEETING RETURNS IN THE IN-PERSON FORMAT

Thursday, 12th May 2022

This year, when the American Association of Clinical Endocrinology (AACE) celebrates their 30th annual meeting they will be doing so in person. Last year's conference was entirely virtual so this return to "normal" is highly anticipated. Program chair Angela M. Leung, MD, shares her thoughts on the return:

"After having deferred our virtual meetings for the last few years, we are excited and very much looking forward to AACE 2022. This conference will be fully in person. With nearly 90 faculty speakers across six concurrent tracks, the in-person live format will allow attendees to hear the latest advances in clinical endocrinology, reconnect, and network with friends and colleagues – a part of our professional lives that I think we all have been missing."

The AACE conference will run from Thursday, May 12 to Saturday, May 14, at the Hilton San Diego Bayfront Hotel, San Diego, CA. Registration for the conference is still open and offers several options, including a premium registration. Besides being able to attend all sessions and presentations, the premium registration lets attendees access some meeting content on-demand through the end of the year – a helpful option to optimize CME credits. Dr. Leung adds, "There are also several new not-to-be-missed sessions, including a women's leadership session and reception, meetups organized by the diversity, equity, and inclusion committee, interactive board reviews, and even endocrine jeopardy."

The Conference Program

The goals of the AACE conference are focused on the clinical needs of the endocrine healthcare professional providing:

- The latest scientific and clinical discoveries in the field of endocrinology, diabetes, and metabolism
- Ways to apply new-found knowledge to the diagnosis and management of endocrine patients for improved outcomes
- Ways to assess the potential applications of emerging scientific advances that affect the practice of endocrinology
- Easy ways to explain the latest clinical treatment options in endocrine health to patients

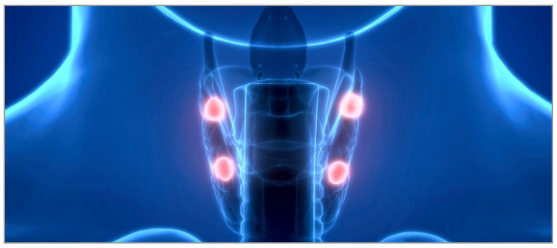
With this in mind, the conference will cover six topics, with plenary presentations by experts in the each field:

DIABETES

"Diabetes Technologies in 2022"

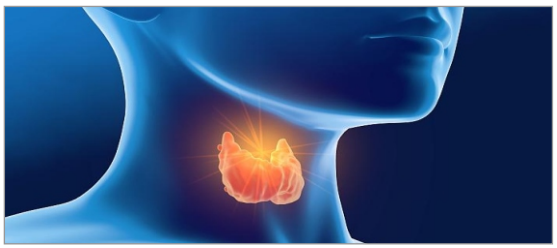
BONE AND PARATHYROID

"Phosphatonins: From Discovery to Therapeutics"



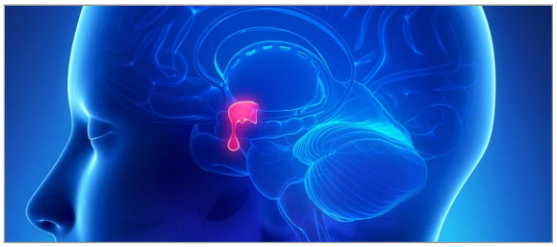
THYROID

"Targeted Therapies in Advanced Thyroid Cancer"



PITUITARY AND NEUROENDOCRINE

"The New Biology of Pheochromocytomas"

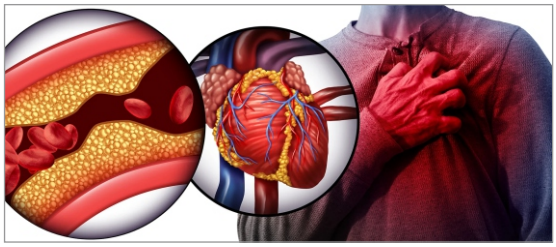


NUTRITION AND OBESITY

"The Gut Hormone-Brain Axis: Mechanisms, Pharmacology, and Treatment in Patients with Adiposity-Based Chronic Disease"

LIPIDS AND CV HEALTH

"Cardiometabolic Effects of Fatty Kidney Disease"



The AACE is returning to an in-person meeting in San Diego, CA. COVID-19 safety measures will follow recommendations by the state government of California, the CDC, and WHO. Therefore, it is important to check these sites before committing to conference plans.

Conference organizers anticipate at least 1,300 attendees with 85 presenters. Advanced registration is open through April 18, with standard registration open afterward. In addition to premium registration, there are tiers for members, non-members, and discounted prices for fellows, residents, and students. Finally, Dr. Leung offers the following encouraging words, "I very much look forward to seeing you all in San Diego this May."

AMERICAN ASSOCIATION OF CLINICAL ENDOCRINOLOGY CLINICAL PRACTICE GUIDELINE FOR THE DIAGNOSIS AND MANAGEMENT OF NONALCOHOLIC FATTY LIVER DISEASE IN PRIMARY CARE AND ENDOCRINOLOGY CLINICAL SETTINGS IN ASSOCIATION WITH AMERICAN ASSOCIATION FOR THE STUDY OF LIVER DISEASES (AASLD)

Thursday, 12th May 2022

This guideline was presented on May 12th at the 30th Annual Meeting of the American Association of Clinical Endocrinology (AACE) at San Diego, by Dr. Kenneth Cusi, MD, FACE, FACP from the University of Florida.

Nonalcoholic fatty liver disease (NAFLD) is the most common cause of chronic liver disease affecting 25% of the global population. Despite the sizable and growing prevalence, disease awareness remains limited with <5% of persons with NAFLD being aware of their disease compared with 38% of persons with viral hepatitis. Twelve to 14% of persons with NAFLD have a more aggressive form known as nonalcoholic steatohepatitis (NASH), which can progress to advanced liver fibrosis, cirrhosis, or liver cancer. The risk of NASH is two- to threefold higher in persons with obesity and/or type 2 diabetes mellitus. NASH is among the top causes of liver cancer and the second most common indication for liver transplantation in the United States after hepatitis C.

NAFLD is diagnosed by abnormal liver test results (although liver test results may be normal) and imaging studies, not related to excess alcohol use or other causes of liver disease. NASH is diagnosed by a liver biopsy; however, specialized blood tests and imaging can determine the risk of significant fibrosis. NAFLD is associated with cardiometabolic disorders:

1) obesity,
2) insulin resistance,
3) type 2 diabetes mellitus
4) high blood pressure, and
5) atherogenic dyslipidemia, all of which increase the risk of a heart attack or stroke, the most common cause of death. The primary treatment of NAFLD is weight loss with a low-calorie diet; restriction of saturated fat, starch, and sugar; improved eating patterns (e.g., Mediterranean diet and minimally processed whole foods); and exercise. Cardiometabolic benefit and reduction of liver fat can be observed with >5% weight loss. More weight loss provides increased benefits and may reverse steatohepatitis or liver fibrosis (≥10% weight loss). There are no U.S. Food and Drug

Administration-approved medications for the treatment of NAFLD; however, some diabetes and antiobesity medications can be beneficial. Bariatric surgery is also effective for weight loss and reducing liver fat in persons with severe obesity.

SUMMARY OF RECOMMENDATIONS

Diagnosis of NAFLD in adults

Q2.1 Which adults with NAFLD should be considered at "high risk" of clinically significant fibrosis (stages F2-F4) and at risk of cirrhosis?

Clinicians should consider persons with obesity and/or features of metabolic syndrome, those with prediabetes or T2D, and those with hepatic steatosis on any imaging study and/or persistently elevated plasma aminotransferase levels (over 6 months) to be "high risk" and screen for NAFLD and advanced fibrosis.

Grade B; Intermediate/High Strength of Evidence; BEL 2

Persons undergoing bariatric surgery should be evaluated for the presence and severity of NASH, and a liver biopsy should be considered at the time of bariatric surgery. Liver biopsy should be recommended if presurgical stratification suggests indeterminate or high risk of liver fibrosis.

Table
Causes of Secondary Hepatic Steatosis and Laboratory Evaluation for the Secondary Causes of Liver Disease

Causes
- Excessive alcohol consumption
- Hepatitis C (genotype 3)
- Lipodystrophy
- Acute weight loss (bariatric surgery and starvation)
- Malnutrition
- Parenteral nutrition
- Abetalipoproteinemia
- Reye syndrome
- Pregnancy associated
  - HELLP syndrome
  - Acute fatty liver of pregnancy
- Medications (eg, corticosteroids, mipomersen, lomitapide, amiodarone, methotrexate, tamoxifen, valproate, and antiretroviral medicines)
- Rare causes: autoimmune hepatitis, A1AT deficiency, Wilson syndrome, and other

Laboratory evaluation
- Hepatitis C
  - HCV antibody with reflex testing HCV RNA
- Additional tests to consider:
  - Hepatitis B: HBsAg, HBsAb, and HBcAb[b]
  - ANA
  - AMA
  - ASMA
  - Immunoglobulins
  - Ferritin
  - A1AT

Grade B; Intermediate Strength of Evidence; BEL 2

Q2.2 What blood tests (eg, diagnostic panels and specific biomarkers) can be used to diagnose NAFLD with clinically significant fibrosis (stages F2-F4) in adults?

R2.2.1 Clinicians should use liver fibrosis prediction calculations to assess the risk of NAFLD with liver fibrosis. The preferred noninvasive initial test is the FIB-4.

Grade B; Intermediate Strength of Evidence; BEL 2

Clinicians should consider persons belonging to the "high-risk" groups (as defined under R2.1.1) who have an indeterminate or high FIB-4 score for further workup with an LSM (transient elastography) or ELF test, as available.

Grade B; Intermediate Strength of Evidence; BEL 2

Q2.3 What imaging studies can be used to diagnose NAFLD with clinically significant fibrosis (stages F2-F4) in adults?

To stage the risk of fibrosis in persons with NAFLD, clinicians should prefer the use of VCTE as best validated to identify advanced disease and predict liver-related outcomes. Alternative imaging approaches may be considered, including shear wave elastography (less well validated) and/or magnetic resonance elastography (most accurate but with a high cost and limited availability; best if ordered by liver specialist for selected cases).

Grade B; Intermediate Strength of Evidence; BEL 2

Table
Additional Causes of Elevated Aminotransferase Levels

- Medications, vitamins, and supplements
- Viral hepatitis (A, B, and C)
- Endocrine disorders (hyper- or hypothyroidism, Cushing syndrome, hypogonadism, growth hormone deficiency, Addison's disease, and other)
- Hemochromatosis
- Autoimmune hepatitis
- Primary biliary cholangitis
- Alpha-1 antitrypsin deficiency
- Budd-Chiari syndrome
- Mass lesions

Q2.4 Should all persons with diabetes mellitus be screened for clinically significant fibrosis (stages F2-F4) associated with NAFLD?

In persons with T2D, clinicians should consider screening for clinically significant fibrosis (stages F2-F4) using the FIB-4, even if they have normal liver enzyme levels.

Grade B; High/Intermediate Strength of Evidence; BEL 2

R2.4.2 In persons with T1D, clinicians may consider screening for NAFLD with clinically significant fibrosis (stages F2-F4) using the FIB-4, only if there are risk factors such as obesity, features of metabolic syndrome, elevated plasma aminotransferase levels (>30 U/L), or hepatic steatosis on imaging.

Grade C; Intermediate/Weak Strength of Evidence; BEL 2; downgraded based on the heterogeneity of studies and moderate to high probability of bias

R2.4.3 Clinicians should further risk stratify persons with T2D, or T1D with cardiometabolic risk factors and/or elevated plasma aminotransferase levels (>30 U/L) using the FIB-4, elastography, and/or ELF test.

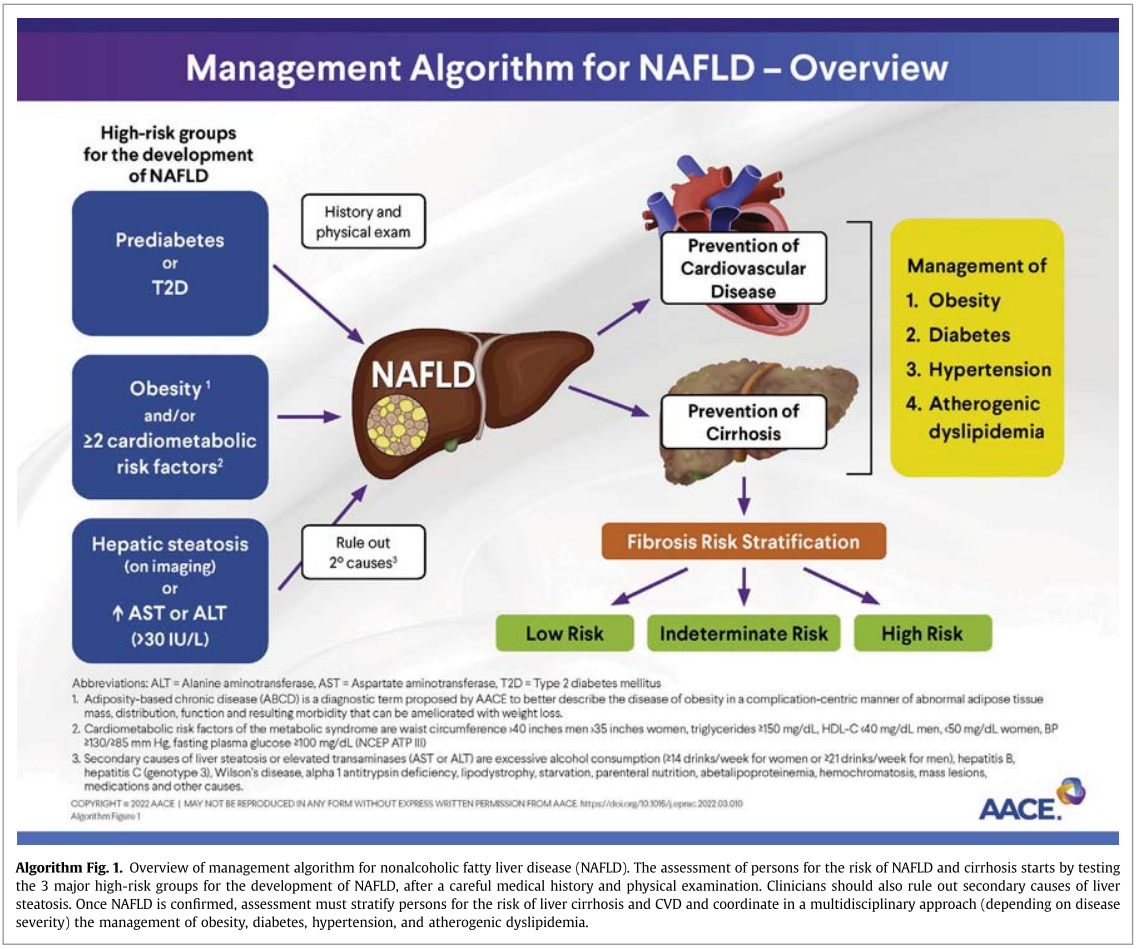
Grade B; High/Intermediate Strength of Evidence; BEL 2

Q2.5 When should an adult be referred to a gastroenterologist/hepatologist for management?

Persons with persistently elevated ALT or AST levels and/or with hepatic steatosis on imaging and indeterminate risk (FIB-4, 1.3-2.67; LSM, 8-12 kPa; or ELF test, 7.7-9.8) or high risk (FIB-4, >2.67; LSM, >12 kPa; or ELF test, >9.8) based on blood tests and/or imaging (as described in R2.2.1, R2.2.2, and R2.3) should be referred to a gastroenterologist or hepatologist for further assessment, which may include a liver biopsy.

Grade B; Intermediate Strength of Evidence; BEL 2

R2.5.2 Clinicians should refer persons with clinical evidence of advanced liver disease



Algorithm Fig. 1. Overview of management algorithm for nonalcoholic fatty liver disease (NAFLD). The assessment of persons for the risk of NAFLD and cirrhosis starts by testing the 3 major high-risk groups for the development of NAFLD, after a careful medical history and physical examination. Clinicians should also rule out secondary causes of liver steatosis. Once NAFLD is confirmed, assessment must stratify persons for the risk of liver cirrhosis and CVD and coordinate in a multidisciplinary approach (depending on disease severity) the management of obesity, diabetes, hypertension, and atherogenic dyslipidemia.

(ascites, hepatic encephalopathy, esophageal varices, or evidence of hepatic synthetic dysfunction) to a gastroenterologist/ hepatologist for further care.

Grade B; Intermediate/High Strength of Evidence; BEL 2

Management of NAFLD in adults

Q3.1 How should cardiometabolic risk and other extrahepatic complications be managed in the setting of NAFLD?

Clinicians must manage persons with NAFLD for obesity, metabolic syndrome, prediabetes, diabetes mellitus, dyslipidemia, hypertension, and CVD based on the current standards of care.

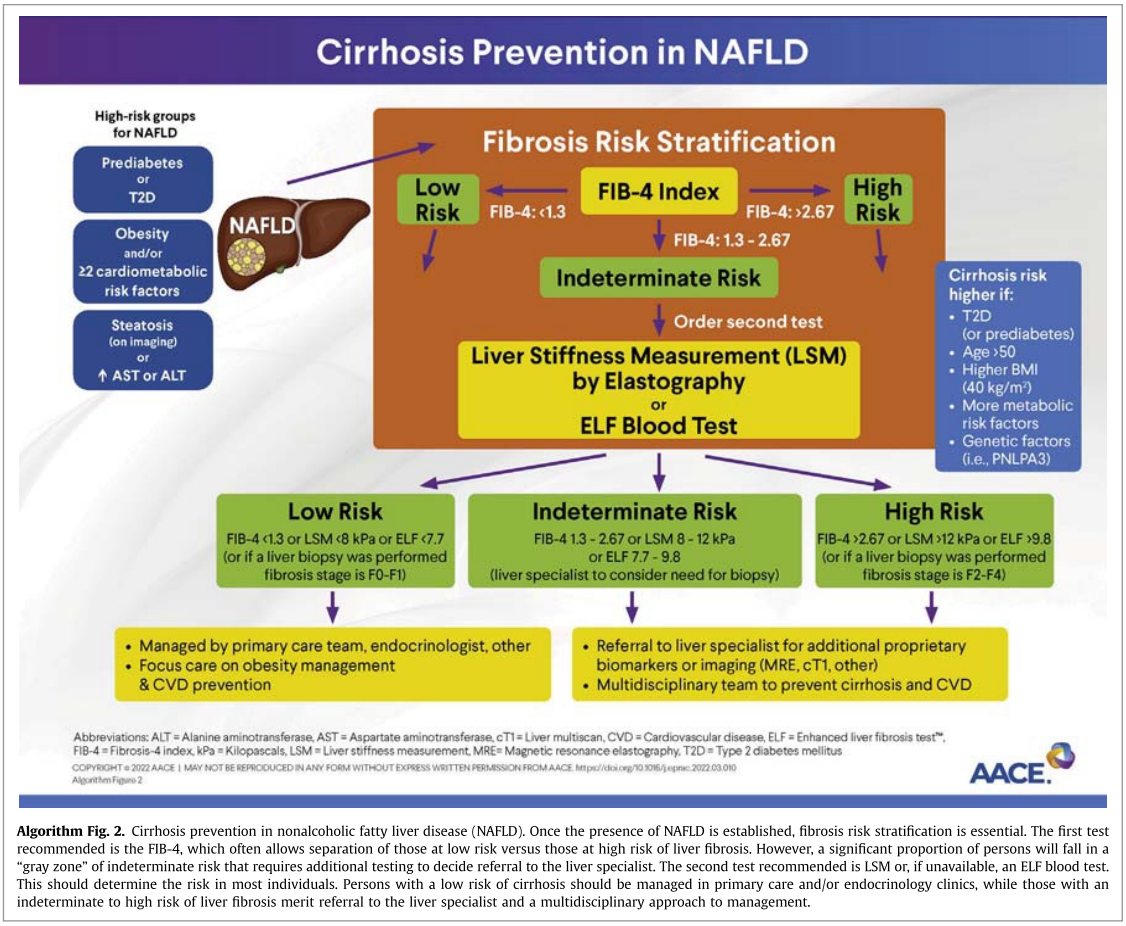
Grade A; High/Intermediate Strength of Evidence; BEL 1

Q3.2 What lifestyle modifications (dietary intervention and exercise) should be recommended in adults with NAFLD?

Clinicians should recommend lifestyle changes in persons with excess adiposity and NAFLD with a goal of at least 5%, preferably ≥10%, weight loss, as more weight loss is often associated with greater liver histologic and cardiometabolic benefit, depending on individualized risk assessments. Clinicians must recommend participation in a structured weight loss program, when possible, tailored to the individual's lifestyle and personal preferences.

Grade B; Intermediate/High Strength of Evidence; BEL 1; downgraded due to small sample sizes, large heterogeneity of interventions, short duration, and few studies with liver biopsy

Clinicians must recommend dietary modification in persons with NAFLD, including a reduction of macronutrient content to induce an energy deficit (with restriction of saturated fat, starch, and added sugar) and adoption of healthier eating patterns, such as the Mediterranean diet.



Algorithm Fig. 2. Cirrhosis prevention in nonalcoholic fatty liver disease (NAFLD). Once the presence of NAFLD is established, fibrosis risk stratification is essential. The first test recommended is the FIB-4, which often allows separation of those at low risk versus those at high risk of liver fibrosis. However, a significant proportion of persons will fall in a "gray zone" of indeterminate risk that requires additional testing to decide referral to the liver specialist. The second test recommended is LSM or, if unavailable, an ELF blood test. This should determine the risk in most individuals. Persons with a low risk of cirrhosis should be managed in primary care and/or endocrinology clinics, while those with an indeterminate to high risk of liver fibrosis merit referral to the liver specialist and a multidisciplinary approach to management.

Grade A; Intermediate Strength of Evidence; BEL 1
R3.2.3 In persons with NAFLD, clinicians must recommend physical activity that improves body composition and cardiometabolic health. Participation in a structured exercise program should be recommended, when possible, tailored to the individual's lifestyle and personal preferences.

Grade A; Intermediate Strength of Evidence; BEL 1

Q3.3 What medications have proven to be effective for the treatment of liver disease and cardiometabolic conditions associated with NAFLD or NASH?
R3.3.1a Pioglitazone and GLP-1 RAs are recommended for persons with T2D and biopsy-proven NASH.

Grade A; High Strength of Evidence; BEL 1
R3.3.1b Clinicians must consider treating diabetes with pioglitazone and/or GLP-1 RAs when there is an elevated probability of having NASH based on elevated plasma aminotransferase levels and noninvasive tests.

Grade A; High Strength of Evidence; BEL 1
R3.3.2 To offer cardiometabolic benefit in persons with T2D and NAFLD, clinicians must consider treatment with GLP-1 RAs, pioglitazone, or SGLT2 inhibitors; however, there is no evidence of benefit for treatment of steatohepatitis with SGLT2 inhibitors.

Grade A; High Strength of Evidence; BEL 1
R3.3.3 Due to the lack of evidence of efficacy, metformin, acarbose, dipeptidyl peptidase IV inhibitors, and insulin are not recommended for the treatment of steatohepatitis (no benefit on hepatocyte necrosis or inflammation) but may be continued as needed for the treatment of hyperglycemia in persons with T2D and NAFLD or NASH.

Grade B; High Strength of Evidence; BEL 1; downgraded due to the use of surrogate outcome measures in many of the studies
R3.3.4 Vitamin E can be considered for the treatment of NASH in persons without T2D, but there is not enough evidence at this time to recommend for persons with T2D or advanced fibrosis.

Grade B; High Strength of Evidence; BEL 1; downgraded due to risk/benefit
R3.3.5 Other pharmacotherapies for persons with NASH cannot be recommended at the present time due to the lack of robust evidence of clinical benefit.

Grade A; High Strength of Evidence; BEL 1

What obesity pharmacotherapies have proven benefit for the treatment of liver disease and cardiometabolic conditions associated with NAFLD or NASH in adults?
R3.4.1 Clinicians should recommend the use of obesity pharmacotherapy as adjunctive therapy to lifestyle modification for individuals with obesity and NAFLD or NASH with a goal of at least 5%, preferably ≥10 %, weight loss, as more weight loss is often associated with greater liver histologic and cardiometabolic benefit, when this is not effectively achieved by lifestyle modification alone.

Grade B; Intermediate Strength of Evidence; BEL 1; downgraded due to small sample sizes used in studies and short duration of trials
For chronic weight management in individuals with a BMI of ≥27 kg/m2 and NAFLD or NASH, clinicians should give preference to semaglutide 2.4 mg/week (best evidence) or liraglutide 3 mg/day.

Grade B; High/Intermediate Strength of Evidence; BEL 1; downgraded due to different formulations and doses used in the semaglutide and liraglutide NASH trials
Clinicians must consider obesity pharmacotherapy (with preference to semaglutide 2.4 mg/week [best evidence] or liraglutide 3 mg/day) as adjunctive therapy to lifestyle modification for individuals with obesity and NAFLD or NASH to promote cardiometabolic health and treat or prevent T2D, CVD, and other end-stage manifestations of obesity.

Grade A; High/Intermediate Strength of Evidence; BEL 1

Q3.5 What is the effect of bariatric surgery on liver disease and cardiometabolic conditions associated with NAFLD or NASH in adults?
Clinicians should consider bariatric surgery as an option to treat NAFLD (Grade B; Intermediate/Weak Strength of Evidence; BEL 2) and improve cardiometabolic health (Grade A; High/Intermediate Strength of Evidence; BEL 2; upgraded based on the cardiometabolic and all-cause mortality benefits in all persons with or without NAFLD) in persons with NAFLD and a BMI of ≥35 kg/m2 (≥32.5 kg/m2 in Asian populations), particularly if T2D is present. It should also be considered an option in those with a BMI of ≥30 to 34.9 kg/m2 (≥27.5 to 32.4 kg/m2 in Asian populations)

(Grade B; Intermediate/Weak Strength of Evidence; BEL 2).
R3.5.2 For persons with NASH and compensated cirrhosis, clinicians should exercise caution in recommending bariatric surgery, which should be highly individualized if prescribed and performed at experienced centers

(Grade B; Intermediate/Weak Strength of Evidence; BEL 2).
In persons with decompensated cirrhosis, bariatric surgery should not be recommended due to limited evidence and potential for harm

(Grade B; Intermediate/Weak Strength of Evidence; BEL 2).

Table
Immunizations for Persons With Chronic Liver Disease

Hepatitis A vaccine
Hepatitis B vaccine
Pneumococcal polysaccharide vaccine (PPSV23)
Additional vaccines:
• Influenza vaccine
• Tdap vaccine
• Zoster vaccine
• HPV vaccine
• MMR vaccine
• Varicella vaccine
• COVID-19 vaccine

R3.5.3 Endoscopic bariatric and metabolic therapies and orally ingested devices should not be recommended in persons with NAFLD due to insufficient evidence.

Grade C; Intermediate/Weak Strength of Evidence; BEL 2; downgraded due to the quality of studies and small sample sizes

Diagnosis and management of children with NAFLD

Q4.1 Who should be screened for NAFLD and comorbidities?
Children of any age and adolescents with obesity or T2D, but not T1D, should be screened for NAFLD using serum ALT.

Grade B; Intermediate/High Strength of Evidence; BEL 2
R4.1.2 Clinicians should screen adolescent females with polycystic ovary syndrome for NAFLD using serum ALT.

Grade B; Intermediate/High Strength of Evidence; BEL 2
R4.1.3 Clinicians should screen children and adolescents with NAFLD for prediabetes or T2D using an oral glucose tolerance test if the fasting glucose level is ≥100 mg/mL or if the glycated hemoglobin (A1c) level is in the range of prediabetes (≥5.7% to 6.4%).

Grade B; Intermediate Strength of Evidence; BEL 2

Q4.2 What tests can be used to diagnose pediatric NAFLD?
R4.2.1 Clinicians should use plasma aminotransferases to test children at high risk of NAFLD.

Grade B; Intermediate Strength of Evidence; BEL 2
R4.2.2 Pediatric NAFLD can be diagnosed with imaging (ultrasound or magnetic resonance imaging-proton density fat fraction) or liver biopsy, in combination with exclusion of non-NAFLD causes of hepatic steatosis such as Wilson syndrome, mitochondrial disease, and medications.

Table
Medications to Treat Diabetes and Their Efficacy for the Treatment of Nonalcoholic Fatty Liver Disease

Medication	Liver fat	Disease activity (steatohepatitis/NAS)	Studies
Metformin	Unchanged	Neutral	(298-302)
Pioglitazone	Decreased	Improved[a]	(97, 98, 280-282)
Insulin	Decreased	Effect unknown	(177, 178, 306)
GLP-1 RAs (semaglutide and liraglutide)	Decreased	Improved[a]	(99, 286-288)
SGLT2 inhibitors (dapagliflozin, empagliflozin, and canagliflozin)	Decreased	Effect unknown	(28, 294-297)
DPP-IV inhibitors (sitagliptin and vildagliptin)	Unchanged (in RCTs)	Effect unknown	(286, 303-305)

Grade B; Intermediate Strength of Evidence; BEL 2
R4.2.3 Liver fibrosis prediction calculations and proprietary biomarkers currently available for the diagnosis of advanced fibrosis in adults should not be used in children as they either are inaccurate or require further validation.

Grade B; Intermediate Strength of Evidence; BEL 2

Q4.3 What are the lifestyle, medical, or surgical treatment options for pediatric NAFLD, and what is the role of pharmacotherapy developed for endocrine disorders in the treatment of pediatric NAFLD?

Clinicians should recommend lifestyle changes in children with NAFLD, promoting the adoption of dietary changes to create an energy deficit, with reduction in sugar consumption as first-line lifestyle modification and increased physical activity aiming for BMI optimization.

Grade B; Intermediate Strength of Evidence; BEL 1; downgraded due to the limited number of RCTs and small sample sizes
R4.3.2 Clinicians may consider GLP-1 RAs for the treatment of pediatric obesity and T2D

(Grade D; Expert Opinion; BEL 4), which may also offer benefit for pediatric NAFLD, although not FDA-approved for this indication (Grade D; Expert Opinion; BEL 4).

Table
BMI-for-Age Weight Status Categories in Children and Adolescents and the Corresponding Percentiles

Weight status category	BMI percentile range
Underweight	<5th percentile
Healthy weight	5th percentile to <85th percentile
Overweight	85th to <95th percentile
Obesity class I	≥95th percentile to <120% of the 95th percentile for age and sex
Obesity class II	≥120% to <140% of the 95th percentile or BMI ≥ 35 kg/m^2
Obesity class III	≥140% of the 95th percentile or BMI ≥ 40 kg/m^2

SESSION-5: EXERCISE IS MEDICINE: ENERGY EXPENDITURE ACROSS THE LIFESPAN

EXERCISE IS MEDICINE: ENERGY EXPENDITURE ACROSS THE LIFESPAN

Thursday, 12th May 2022

Exercise for Cardiometabolic Health and Obesity by John M. Jakicic, PhD, Professor University of Kansas Medical Center, Center for Physical Activity and Weight Management Kansas City, Kansas, United States.

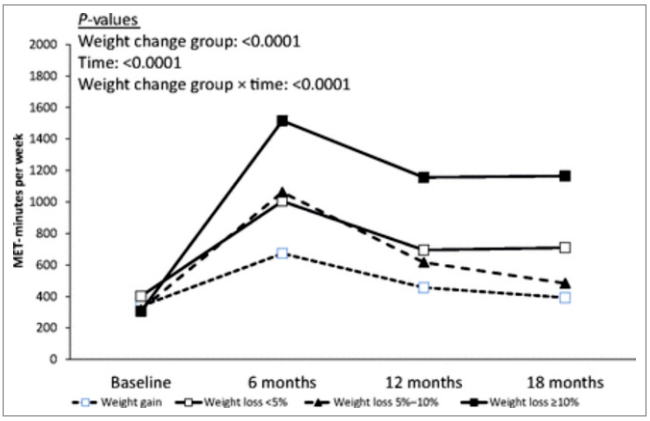
Overweight and obesity are significant public health concerns that are linked to numerous negative health consequences. Physical activity is an important lifestyle behavior that contributes to body weight regulation.

Physical activity is inversely associated with weight gain and the incidence of obesity. Physical activity also contributes to additional weight loss when coupled with dietary modification, and it can result in modest weight loss when not coupled with dietary modification. Moreover, physical activity is associated with improved long-term weight loss and prevention of weight gain following initial weight loss. Current evidence supports that physical activity should be moderate to vigorous in intensity to influence body weight

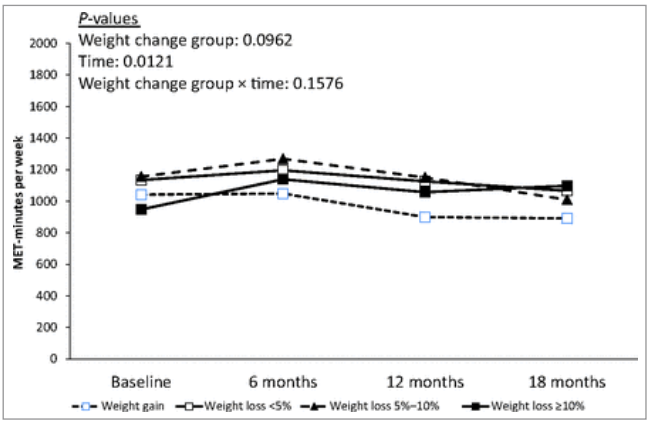
regulation. There is also a growing body of evidence that physical activity can be accumulated throughout the day in shorter periods of time rather than being performed during a structured and longer period, and that physical activity performed in this manner can be important for body weight regulation.

The literature supports the inclusion of physical activity as an important lifestyle behavior for regulating body weight. There are multiple intervention approaches that may be effective for enhancing physical activity engagement within the context of weight control.

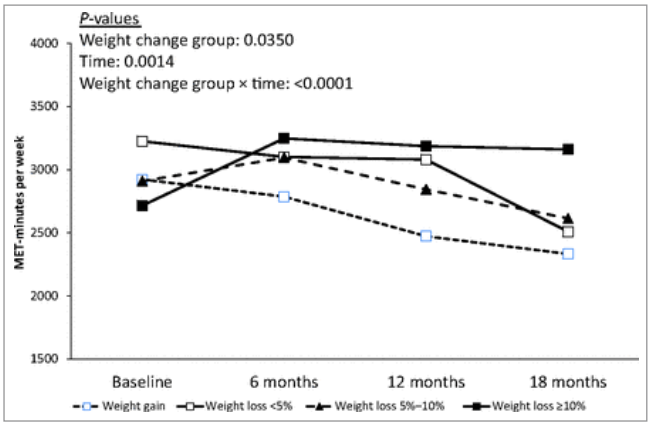
Change in moderate-to-vigorous intensity physical activity (bouts ≥10 min in duration) by weight loss achieved at 18 months.



Change in moderate-to-vigorous intensity physical activity (bouts ≤10 min in duration) by weight loss achieved at 18 months.



Change in light-intensity physical activity by weight loss achieved at 18 months.



Dr. John highlighted the role of exercise in managing cardiometabolic health and obesity. He highlighted that interrupting prolonged sitting with light activity breaks, such as short walks, improves cardiometabolic outcomes, yet less is known about the impact of resistance exercise breaks. A study examined the effects of hourly, guidelines-based simple resistance exercise breaks on acute cardiometabolic health outcomes over a simulated work period. Fourteen adults (age: 53.4 ± 9.5 years, body mass index: 30.9 ± 4.8 kg/m2) completed 2 randomized 4-h conditions: prolonged sitting (SIT) and hourly resistance exercise breaks (REX). Glucose, triglycerides, blood pressure, and heart rate were measured at baseline and then hourly. Pulse wave velocity (PWV) was measured before and after each condition. Linear mixed models evaluated overall condition effects and differences at each hour. Cohen's d estimated magnitude of effects. Four-hour glucose area under the curve (AUC) did not differ by condition (REX vs. SIT: $\beta = -0.35$ mmol/L, $p = 0.278$, $d = 0.51$). However, an attenuation of postprandial glucose at 1 h ($\beta = -0.69$ mg/dL, $p = 0.004$, $d = 1.02$) in REX compared with SIT was observed. Triglyceride AUC, mean blood pressure, and PWV did not differ significantly between REX and SIT overall or any time point (all $p > 0.05$). Heart rate was higher across the experimental period in REX versus SIT ($\beta = 3.3$ bpm, $p < 0.001$,

d = 0.35) and individual time points (β ≥ 3.2 bpm, p ≤ 0.044, d ≥ 0.34). Resistance exercise breaks can potentially improve 1-h postprandial glucose, but may not acutely benefit other cardiometabolic outcomes.

Importance of Physical Activity in Reducing Cardiometabolic Risk

In addition to the benefits on weight loss and prevention of weight gain, physical activity of sufficient dose and intensity will improve cardiorespiratory fitness in adults who are overweight or obese. The improvements in fitness usually occur in a dose–response manner, with greater improvements observed as volume and intensity of physical activity increase. The improvement in cardiorespiratory fitness has been shown to be associated with a variety of health-related benefits that include reduced mortality, which may occur independent of the level of BMI or body fatness. Moreover, cardiorespiratory fitness may also be associated with improvements in a variety of cardiometabolic risk factors, such as blood pressure and glycemic control. These findings suggest that physical activity, partially through its impact on cardiorespiratory fitness, may have important health implications beyond the management of body weight in adults who are overweight or obese.

Related to this area is the "obesity paradox," which suggests that for some health-related conditions there may be a protective effect of obesity rather than a detrimental effect. Recent meta-analyses and systematic reviews have supported this position, which may suggest that interventions should focus on enhancing physical activity behavior rather than on weight loss. However, there is debate in the literature on this topic, with some investigators suggesting that there may be confounding bias that results in the presence of the "obesity paradox". Thus, this may indicate the need for additional research specifically targeting whether there are health-related conditions for which excess body weight may have a protective effect, and these studies should consider the influence that physical activity and cardiorespiratory fitness may have on these relationships.

ENERGY EXPENDITURE, BODY COMPOSITION, AND OBESITY

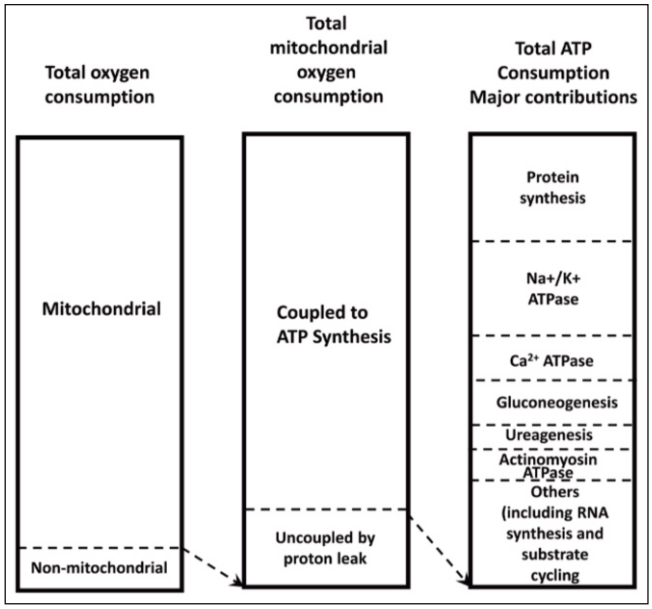
Thursday, 12th May 2022

Dr. Eric Ravussin, Associate Executive Director Pennington Biomedical Baton Rouge, United States.

Although many individuals achieve weight loss of 10% or more, the ability to maintain a reduced body mass over months and years is much rarer. Unfortunately, our understanding of the adverse consequences of having overweight and obesity argues that long-term maintenance of a reduced weight provides the greatest health benefit. However, to achieve long-term weight reduction requires overcoming neuroendocrine systems that favor restoration of one's initial weight. Identifying and characterizing the components of these systems will be important if we are to develop therapies and strategies to reduce the rates of obesity and its complications in our modern society. During this session, Eric Ravussin discussed the physiology of the weight-reduced state that favors weight regain and a molecular component that contributes to this response.

Estimated contribution of processes to energy utilization. The first column shows the contribution of mitochondrial to non-mitochondrial oxygen consumption to total respiration. Second column shows the proportion of used to drive ATP synthesis versus proton leak. The third column represents the contribution of ATP consuming processes to total ATP production.

The session attempted to briefly review key concepts in the assessment of energy expenditure in the weight-reduced state that



point to known and potential mechanisms and regulators of efficiency (hormones such as leptin and T3, as well as mitochondrial and nonmitochondrial control systems) as a source of the observed decreased energy waste and decreased heat production. Many other potential mechanisms are still likely to be discovered. The challenge will be to parse out the interconnectedness and the individual contribution of these pathways to the ability to lose weight and to maintain weight loss. Future studies should aspire to collect data on the activity of as many of these systems as possible in order to develop rational strategies to achieve and maintain weight loss when desirable to improve health.

In summary, based on our present knowledge, we can draw distinct lessons that may help those people struggling to maintain a healthier weight in our modern obesogenic environment:

1. Weight loss, and even dramatic weight loss, is indeed possible. However, the kind of weight loss achieved in "The Biggest Loser" (except maybe for those obtained via bariatric surgery) is almost impossible to maintain when individuals return to their natural environment in the absence of constant therapeutic support.
2. The major drivers of weight regain are the well-established physiological responses to weight loss, i.e., the persistence of a lower RMR, lower energy cost of weight-bearing activities, decreased fat oxidation, and persistence of increased appetite related to long-lasting increased orexigenic and decreased anorexic signals.
3. Only those who engage in high levels of physical activity after weight loss have been successful in maintaining a reduced weight.

SESSION-6: DIABETES AND HYPOGLYCEMIA

ADULTS WITH TYPE 1 DIABETES ON MULTIPLE DAILY INJECTIONS CAN ACHIEVE BETTER GLYCEMIC CONTROL WITHOUT WORSENING HYPOGLYCEMIA USING THE MINIMED 670G HYBRID CLOSED-LOOP SYSTEM

Thursday, 12th May 2022

This paper was presented on May 12th at the 30th Annual Meeting of the American Association of Clinical Endocrinology (AACE) at San Diego, by Drs. Hamda Ali, M Dabia Al-Mohanadi, MD, FRCPC Ameena Al-Abdulla, Ba Kawsar Mohamud, Bc Judith Campbell, Bc Goran Petrovski, MD, MSc, PhD from the Hamda Medical Corporation.

The MiniMed 670G hybrid closed-loop (HCL) system was the first FDA-approved automated insulin delivery system for patients with type 1 diabetes (T1D). We aimed in this study to evaluate a 10-day initiation protocol in adults with T1D from multiple daily injections (MDI) to MiniMed 670G HCL system in achieving glycemic control.

"We recruited individuals with T1D on MDI, aged 18-65 years with HbA1C less than 12.5% (113 mmol/mol) in an open-label, single-arm study for 3 months. The primary outcome was achievable Time in Range (TIR), 3.9-10 mmol/L (70-180 mg/dL), over the first 84 days after initiation of the Auto Mode of the HCL system. The participants went through a planned 10-day protocol of 2 days to assess their readiness for the HCL system, followed by 5 days of system training in groups of 3-5 individuals, then 3 days of Manual Mode use before starting the Auto Mode. We collected the real-time continuous glucose monitoring (CGM) data at baseline and the CGM, pump settings, and system usage data over the first 84 days of Auto Mode use. Statistical analysis was performed using STATISTICA 12 (StatSoft, Tulsa, USA)."

We enrolled 24 individuals (13 females), aged 28.8±9 years with T1D for 12.1±7.4 years, mean HbA1C of 8.9±1.4% (74±15.3 mmol/mol), TIR of 48.96±17.9%, time below range (TBR) of 5.96±7.6%, and time above range (TAR) of 43.42±16.8%. One female did not complete the study as she became pregnant. During the first 84 days on the Auto mode of the HCL system, the participants had a median sensor usage of 86% of the time and spent a median time of 83% in Auto Mode. TIR increased to 67.22±13.2% (P = 0.0003), TBR decreased to 3.57±2.9% (P = 0.16), and TAR decreased to 29.22±13.2% (P = 0.0024). The mean HbA1C improved to 7.5±0.8% (59±9.3 mmol/mol) by the end of the study (P = 0.0001). No diabetic ketoacidosis or severe hypoglycemia episodes were recorded during the study.

Previous studies on MiniMed 670G recruited participants with previous insulin pump experience, while our patients were insulin pump naïve. We used the same 10-day onboarding protocol that was tested before to initiate the 670G HCL system in a study of the pediatric age group reaching a TIR of 75.6±6.9% three months after initiation. The adult participants in our study had significant improvement in HbA1C and TIR, although it was less than what was reported in the pediatric population and this could be related to the conduction of the study during the COVID-19 pandemic. The 670G HCL system improved glycemic control without worsening TBR.

ACHIEVEMENT OF HBA1C <6.5% WITH ≥5% WEIGHT LOSS AND WITHOUT HYPOGLYCEMIA IN PATIENTS WITH TYPE 2 DIABETES TREATMENT WITH TIRZEPATIDE: A POST HOC ANALYSIS OF THE SURPASS-1 TO -5 STUDIES

Thursday, 12th May 2022

This paper was presented on May 12th at the 30th Annual Meeting of the American Association of Clinical Endocrinology (AACE) at San Diego, by Drs. Vivian Thieu, PhD Ildiko Lingvay, MD, MPH, MSCS Pratik Choudhary, MD Sheryl Allen, MD Kari Ranta, MD Joshua Levine, MD, PhD. from the Diabetes Research Centre, University of Leicester, Leicester, U and Eli Lilly and Company.

Tirzepatide (TZP) is a dual GIP and GLP-1 receptor agonist developed for the treatment of patients with type 2 diabetes (T2D). The SURPASS clinical trials showed that patients treated with TZP had greater HbA1c and bodyweight reductions compared to placebo

and active comparator treatments and 66% to 95% of participants treated with TZP achieved a HbA1c ≤6.5% at the end of the trials. Additionally, 54% to 88% of participants treated with TZP achieved a body weight loss of ≥5% at the end of the trial and treatment with TZP was not associated with an increase in hypoglycemia vs comparators. This post hoc analysis evaluated the proportion of participants in the SURPASS-1 to -5 studies achieving a triple composite of HbA1c < 6.5% with ≥5% weight loss and without clinically significant hypoglycemia or severe hypoglycemia.

"We compared the proportion of participants achieving the triple endpoint between different doses of TZP (5 mg, 10 mg, 15 mg) and respective study active comparators or placebo groups while patients were on treatment and without rescue medication. End of treatment HbA1c and weight were evaluated at week 40 for SURPASS-1, 2 and 5; and week 52 for SURPASS-3 and 4. Hypoglycemia was defined as blood glucose < 54 mg/dL in the presence of symptoms or severe hypoglycemia."

In all 5 SURPASS studies, significantly more participants treated with any dose of TZP achieved the triple endpoint ($p < 0.05$) compared to placebo or active comparators. As monotherapy, TZP treatment (5, 10, 15 mg) led to 55%, 64%, 67% of participants achieving the triple endpoint compared to 2% with placebo (SURPASS-1). As add-on to metformin, TZP treatment (5, 10, 15 mg) led to 56%, 71%, 77% achieving the same compared to 44% with semaglutide 1 mg (SURPASS-2). When compared to basal insulin, TZP treatment (5, 10, 15 mg) led to 51%, 70%, 77% achieving the triple endpoint compared to 4% with degludec (SURPASS-3; add-on to metformin) and when added to 1-3 oral antihyperglycemics, TZP treatment (5, 10, 15 mg) led to 44%, 61%, 69% achieving the triple endpoint compared to 3% with glargine U100 (SURPASS-4). Finally, as add-on to basal insulin, TZP treatment (5, 10, 15 mg) led to 39%, 55%, 71% achieving the triple endpoint compared to 3% with placebo (SURPASS-5).

Significantly more participants treated with TZP achieved a HbA1c < 6.5% with ≥5% weight loss and without hypoglycemia compared to placebo, semaglutide 1 mg, or basal insulin. More than 50% of patients achieved this triple endpoint for TZP 10 and 15 mg doses.

USE OF GLUCAGON-LIKE PEPTIDE 1 RECEPTOR AGONIST THERAPY FOR INPATIENTS WITH TYPE II DIABETES AND CHRONIC KIDNEY DISEASE: A RETROSPECTIVE ANALYSIS

Thursday, 12th May 2022

This paper was presented on May 12th at the 30th Annual Meeting of the American Association of Clinical Endocrinology (AACE) at San Diego, by Drs. Dmitriy Khazron, DO Joshua Fogel, PhD from the NYC Health Hospitals.

The use and overall benefit of non-insulin glucose lowering agents for hospitalized patients is unclear due to limited data. Our study aims to determine the impact and safety of GLP-1 receptor agonist therapy in hospitalized diabetes patients with chronic kidney disease.

Retrospective study of 51 patients using either liraglutide (n=48) or dulaglutide (n=3). We compared glomerular filtration rate (GFR) groups of stages 3-5 and 1-2. The primary outcome was insulin total amount within the last 24 hours in hospital. The secondary outcomes were safety and glucose management.

The GFR stages 3-5 group (M=0.5, SD=0.36) had a significantly lower mean insulin total amount (p=0.01) within the last 24 hours in hospital than the GFR stages 1-2 group (M=0.8,

SD=0.45). There were increased odds for point-of-care glucose reached the target of 140-180 mg/dl within the last 24 hours in hospital for the GFR stages 3-5 group as compared to the GFR stages 1-2 group (OR:4.08, 95% CI:1.05, 15.83, p=0.04). Both GFR groups had minimal adverse events. GLP-1 receptor agonist therapy at discharge was 94.1%.

"In our study, glucose management with GLP-1 receptor agonists is better for patients with GFR stages 3-5 as compared to GFR stages 1-2. Both GFR groups had minimal adverse events. Our study suggests that use of GLP-1 receptor agonists is a safe and potential useful option for inpatient hyperglycemia management."

PROGNOSTIC MARKERS OF NEPHROPATHY IN PATIENTS WITH DUAL METABOLIC SYNDROME DISEASES (ESSENTIAL HYPERTENSIVE DISEASE AND CONCOMITANT TYPE 2 DIABETES MELLITUS)

Thursday, 12th May 2022

This paper was presented on May 12th at the 30th Annual Meeting of the American Association of Clinical Endocrinology (AACE) at San Diego, by Drs. Manoj Chawla, Purvi Chawla, MD from the Lina Diabetes Care Center.

Nephropathy has characteristics for essential hypertensive disease (EHD) and type 2 diabetes mellitus (T2DM). The objective of the research was to study the adverse factors for nephropathy in patients with combined EHD and T2DM.

120 patients (69 females and 51 males), aged 45-69 years were examined. The average age was (58.2±5.7) years. Group I (GI) included 25 patients with treatment-compensated essential hypertensive disease, II stage, 1-2 degree; Group II (GII) - 25 patients with subcompensated type 2 diabetes mellitus (glycated hemoglobin (HbA1C) - from 7.0 to 11.0%); Group III (GIII) - 70 patients with treatment-compensated essential hypertensive disease, II stage, 1-2 degree and concomitant subcompensated type 2 diabetes mellitus (glycated hemoglobin (HbA1C) - from 7.0 to 11.0%). The control group consisted of 20 practically healthy volunteers, 12 (60.0%) females and 8 (40.0%) males, aged (54.7±4.9) years. The groups were randomised according to age, sex, BMI, duration of EHD and T2DM. In addition to general clinical examination conducted; blood levels of lipid, uric acid (UA), tumour necrosis factor alpha (TNF-α), high-sensitivity C-reactive protein (hs-CRP), CTGF and urine levels of neutrophil gelatinase-associated lipocalin (NGAL) were determined using immuno-fermentation methods.

Changes in the kidneys were more pronounced in Group III patients: category A1 albuminuria was detected in 16 (22.86%), category A2 albuminuria - in 47 (67.14%), category A3 albuminuria - in 7 (10.0%); while in Group I patients - category A1 albuminuria was observed in 20.0% and category A2 albuminuria in 32.0% of GI patients; in GII - category A1 albuminuria was seen in 32.0% and category A2 was seen 48.0% of GII patients. Category A3 albuminuria was not seen in either GI or GII patients. The urine albumin/creatinine (A/Cr) ratio in GIII patients exceeded that in GI patients by 2.56 times, and that of GII patients by 1.45 times ($p < 0.05$). The lowest GFR was in GIII patients and was (69.5±3.6) ml/min/1.73m^2, which was lower than that in the control group by 36.06% ($p < 0.05$), in GI patients - by 26.14% ($p < 0.05$), in GII patients - by 11.35% ($p < 0.05$). More pronounced nephropathy in the presence of EHD and T2DM was indicated by an increase in urinary NGAL levels in GIII patients up to (30.22±1.60) ng/ml, which was higher than the levels in the control group by 4.13 times, in GI patients - by 2.68 times; in GII patients - by 1.35 times ($p < 0.05$). Correlations

between systolic blood pressure (SBP) and A/Cr, GFR, NGAL in urine were found (r=+0.39; r=-0.48; r=+0.43; p< 0.05) respectively; between HbA1C and A/Cr, GFR, NGAL in urine - (r=+0.65; r=-0.62; r=+0.71; p< 0.05) respectively.

Prognostic unfavourable factors for nephropathy in essential hypertensive disease (EHD) and concomitant type 2 diabetes mellitus (T2DM) are characterised by increase in albuminuria and NGAL in urine; and with decrease in GFR, increase in systolic blood pressure, hyperglycemia, dyslipidemia, hyperuricemia, subclinical inflammation (with respect to TNF-α and hs-CRP levels in the blood) and with subsequent activation of fibrogenesis due to increased CTGF levels in the blood.

SESSION-7: DISEASE STATE NETWORK YEAR-IN-REVIEW: NUTRITION AND OBESITY

USE OF CONTINUOUS GLUCOSE MONITOR (CGM) AS A MOTIVATIONAL DEVICE FOR LIFESTYLE MODIFICATIONS TO IMPROVE GLYCEMIC CONTROL IN PATIENTS WITH TYPE 2 DIABETES TREATED WITH NON-INSULIN THERAPIES

Thursday, 12th May 2022

This guideline was presented on May 12th at the 30th Annual Meeting of the American Association of Clinical Endocrinology (AACE) at San Diego, by Drs. Hisham Farhan, MD, Khulood Bukhari, MD, Navneet Grewal Sranita Devarasetty Kashif Munir, MD from the University of Florida.

The efficacy of continuous glucose monitoring (CGM) to improve glycemic control in individuals on intensive insulin therapy has been well established in several studies. There is limited evidence on its efficacy in individuals who are on non-insulin therapies and are unable to achieve glycemic control despite therapeutic advances. CGM has been reported as an effective tool for lifestyle modifications, which is an essential component of type 2 diabetes (T2D) management.

43-year-old man with history of long-standing poorly controlled T2D presented for evaluation. Multiple medication trials failed in the past. He was reluctant to start insulin. At index visit, when his HbA1c was 12.3% on metformin, CGM was initiated along with addition of glipizide. At 3 months, HbA1c improved to 8.1%. He reported his experience with CGM as a "game-changer", as the ability to observe changes in his glucose levels throughout the day provided continuous feedback on food choices and physical activity.

On review of CGM data for the first 2 weeks of initiating CGM, time in range (TIR) was only 13%, but there was a noticeable improvement in daily glycemic values within the first week. At 3 month follow-up, glucose management indicator was 6.7% with TIR of 89%. At 18 months follow up, HbA1c was 7.3% with TIR of 72% indicating the long-term impact of CGM use. Patient reported high level of satisfaction with CGM use with a mean score of 4.0 on benefits subscale and 1.6 on hassles subscale on CGM satisfaction survey.

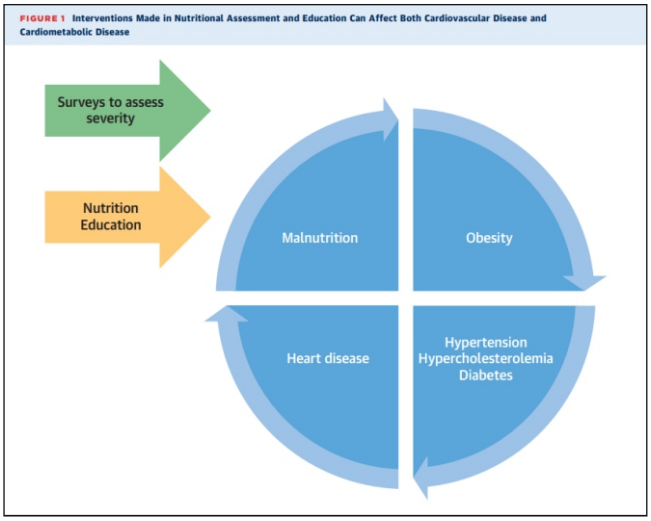
Adherence to lifestyle modifications poses a challenge for most patients. CGM use can be an effective tool in this regard by providing feedback on the effects of diet and exercise on glucose levels. Our patient had long-standing, poorly controlled diabetes, however marked improvement in his glycemic control within weeks of CGM use was demonstrated which was maintained over the following 18 months.

Self-monitoring of blood glucose (SMBG) and HbA1c have historically been the primary methods for assessing glycemic control. CGM use can make SMBG easier by avoiding frequent finger sticks and providing additional information such as time in range, asymptomatic hypoglycemia, and glucose variability. The benefit of remotely sharing CGM data with providers for treatment decisions is another advantage in this era of expanding use of telemedicine. CGM use is associated with high levels of patient satisfaction which can improve quality of life. CGM use in early stages of T2D has the potential to prevent disease progression and long-term complications which can reduce associated healthcare expenditures. Broadening the use of CGM in this patient population will have long-lasting implications.

DISEASE STATE NETWORK YEAR-IN-REVIEW: NUTRITION AND OBESITY

Thursday, 12th May 2022

Dr. Monica, MD, MEHP, FACE – University of Alabama at Birmingham discussed a study which was a retrospective, observational registry study conducted at the University of Vigo, Spain, that looked at 5,062 patients with ACS, of whom 49% of patients were classified as having non–ST-segment elevation myocardial infarction and 40% as having ST segment elevation myocardial infarction. The remainder were classified as having unstable angina. Body mass index (BMI) was calculated for all individuals, and 3 nutritional screening indexes were used (the Controlling Nutritional Status Score, Nutritional Risk Index, and Prognostic Nutritional Index Score). Each nutritional score factors in values such as BMI, albumin level, total lymphocyte count, and/or cholesterol level. Based on these scores, comparison to BMI, and subsequent event rate, strong correlations were found. There are 3 important points that were emphasized in this study. The first notable point is that malnutrition is very



prevalent in patients with ACS and is a real issue in the new millennium, despite BMI, left ventricular function, or coronary revascularization. According to the 3 nutritional risk indices, 50% to 60% of the individuals in this study were classified as malnourished, and between 8.9% and 39.5% of the individuals were classified as moderate-severely malnourished. The second key point is that of the patients who were malnourished, 48% to 58% were overweight or obese (BMI $25 kg/m2), reminding clinicians that more weight does not correlate with food quality and that even these patients are at risk for malnutrition. This is an important concept that needs to be further examined, because this is less widely known. The third message is that malnutrition, regardless of BMI and other risk factors, is associated with increased all-cause mortality and increased major adverse cardiovascular events.

Malnutrition is a largely under-recognized and undertreated condition by clinicians, especially in patients with normal or increased BMI. People often see increased abdominal girth as overnutrition rather than undernutrition. However, poor nutrient quality is an important source of malnutrition and is associated with increased mortality in patients with ACS. The study considers a potential mechanism that nutritional status may be a proxy indicator for inflammation and a trigger for increasing

atherosclerotic burden and higher risk of plaque rupture and ACS.

Recognizing that overweight patients often have poor diet quality can help shift the conversation in the patient-physician visit toward improving nutritional status. Studies have previously shown that eating whole grains, legumes, fruits, vegetables, nuts, and seeds is beneficial in primary and secondary prevention patients in reducing blood pressure, blood glucose, cholesterol, and inflammatory markers. Additional studies have shown that diets rich in these foods can decrease angina and perfusion defects and potentially cause plaque regression. Treatment, then, of a patient at risk must include a nutritional status assessment and counselling on how to shift toward a diet that is rich in these healthier food options. In fact, many of these index hospitalizations for life-threatening events can prove valuable as teaching moments to truly affect care and change treatment trajectories. In outpatient clinic visits where time is limited, surveys such as the 14-point Mediterranean diet survey, Starting the Conversation survey, and 5-question Healthy Eating Vital Sign will help providers recognize malnutrition and poor nutrient quality quickly. Making use of the care team including dieticians, personalized counselling, and community support groups and nutrition educational programs could then be initiated. As has been reported on several occasions, most cardiologists and cardiology care team clinicians lack education and knowledge in nutrition and are therefore less prepared to discuss nutrition and lifestyle measures at the bedside or in the clinic. Paying lip service with the usual phrases, such as "Be sure to exercise and eat right," simply doesn't cut it. It behoves us as a profession to ensure adequate training and competency in the delivery of care in the lifestyle space. Clinicians should be well versed in the dietary patterns known to reduce or even reverse cardiovascular disease (CVD) burden, physical activity guidelines, and the literature and the practice of self-care in the domains of stress relief/mindfulness; connectedness and support; and adequate, good-quality sleep. With each of these lifestyle components, marked improvements in many chronic diseases are possible with minimal cost.

In sum, this study highlights the vast prevalence of malnutrition in patients with ACS. In patients with ACS who experience malnutrition, the rates of mortality are high independent of elevated BMI, ejection fraction, and coronary angiographic findings. These findings should alert clinicians to recognize and assess malnutrition (Figure) in patients who are overweight/obese. Then, helping these identified patients receive adequate education and coaching on fundamental nutrition concepts will help decrease their mortality risk. Furthermore, this paper is yet another urgent call to action: it is time for the CVD profession to arm itself with the most cost effective and powerful tool in the battle against CVD: nutrition and lifestyle medicine.

Dr. Reshmi Srinath, Assistant Professor / Director Weight and Metabolism Management Program Icahn School of Medicine at Mount Sinai, discussed about the dietary management of blood glucose in medical critically ill patients with overweight and obesity. She discussed some of the salient features of her review which are summarized below -

Purpose of review: As the obesity epidemic continues, there is a greater proportion of patients with overweight, obesity, and other forms of adiposity-based chronic disease that require intensive care. Nutrition therapy in the ICU is a vital part of critical care but can be challenging in this setting because of the increased risk of stress hyperglycemia and adverse impact of obesity- and diabetes-related complications.

Recent findings: Current guidelines favor early nutritional therapy with a hypocaloric, high-protein diet in patients with overweight / obesity. More aggressive protein intake may be useful in those with greater severity of

overweight/obesity with an upper limit of 3 g/kg ideal body weight per day. Although there is no specific recommendation, choosing enteral formulas with higher fat content and slower digesting carbohydrates may assist with glucose control. Supplementation with immunonutrients is recommended, given their known benefits in obesity and in reducing inflammation, but must be done in an individualized manner.

Summary: Aggressive nutritional therapy is crucial in patients with overweight/obesity to support ongoing metabolic demands. Although a hypocaloric high-protein feeding strategy is a starting point, nutritional therapy should be approached in an individualized manner taking into account age, weight and BMI, basal metabolism, nutrition status, complications, and comorbidities.

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