The majority of patients in the ILI and DSE groups achieved target BP levels of <130/80 mm Hg (63% vs 60%; p=0.08). Patients in the ILI and DSE groups also had similar improvements in triglyceride levels (-22.90 vs -27.51 mg/dL; p=0.13) and, after controlling for statin use, similar improvements in low-density lipoprotein (LDL) levels (-12.71 vs -13.78 mg/dL; p=0.19). However, patients in the DSE group were more likely than those in the ILI group to achieve an LDL target of <100 mg/dL (64% vs 61%; p=0.02).

Future follow-up analyses will focus on the effects of intentional weight loss on CV events, Dr. Ryan said.

Measures of Central Obesity Are Better than BMI for Understanding Cardiometabolic Risk

Studying abdominal obesity provides important clues on the pathophysiology and natural history of diabetes and cardiovascular disease. Nick Wareham, MD, University of Cambridge, Cambridge, UK, described recent insights on abdominal obesity and cardiometabolic risk from the European Prospective Investigation into Cancer (EPIC).

EPIC is a multinational cohort study that was designed to evaluate the relationships between dietary intake and health outcomes, including cancer, diabetes, and CVD, among more than 500,000 participants. As part of the EPIC study, the EPIC-Norfolk cohort included 25,633 men and women aged 40 to 74 years. According to Prof. Wareham, data from the EPIC-Europe and EPIC-Norfolk cohorts have demonstrated three main benefits in studying central obesity.

Understanding Disease Etiology

Compared with BMI as an index of obesity alone, measures of central obesity are a better indicator of cardiovascular risk. In one EPIC-Norfolk study, waist-to-hip ratio and waist circumference quintiles were stronger predictors of future coronary heart disease than BMI quintiles, even after adjusting for classical CV risk factors.

Genetic studies have identified collections of single-nucleotide polymorphisms that increase the risk of obesity when considered in aggregate. In one EPIC-Norfolk analysis, individuals who carried up to 4 risk alleles had a mean BMI of 25.5 kg/m^2, whereas those with 12 or more risk alleles had a BMI of approximately 27 kg/m^2. However, persons with abundant risk alleles are not necessarily destined for obesity. Indeed, individuals who are genetically predisposed to obesity appear to benefit even more from having an active lifestyle than those with few genetic markers for obesity.

Cardiometabolic Risk Prediction

One reason for developing risk prediction tools is to be able to rank individual risk profiles and target therapy to those who are at greatest risk. For instance, the Framingham Risk Score is used to identify patients who are most likely to benefit from statin therapy because they are at the highest absolute risk. Incorporating measures of abdominal obesity may improve current tools that are used to predict the development of diabetes and CVD. In an EPIC-Europe analysis, waist-to-hip ratio was a better predictor of future diabetes risk than BMI quintile. A tool that includes both BMI and waist-to-hip ratio may be able to identify a subgroup of high-risk patients who are most likely to benefit from treatment to prevent progression to diabetes, Prof. Wareham said.

Risk prediction tools can also be used to motivate patients to change their behavior. For example, one simple tool allows patients to calculate their "heart age," which may differ from their chronological age, based on risk factors, such as cholesterol level, blood pressure, BMI, and smoking history. After learning that their "heart age" may be higher than expected, patients may be more motivated to adhere to therapeutic lifestyle changes. We not only need to investigate what risk information is presented, but also how different ways of presenting risk in a numerical format can influence patient behavior. Going beyond the presentation of numbers, it is possible that visual imaging of the harm that an individual is doing to themselves by adverse lifestyles may also play a role. Patients shown images of their own smoking-related harm, such as an arterial scan showing an atheroma, are more likely to cease smoking. It is possible that a similar tool that highlights a patient's degree of regional adiposity may motivate them to improve adherence to lifestyle interventions.

Demonstrating Response to Interventions

Waist circumference and waist-to-hip ratio may overtake BMI as the preferred tools for demonstrating response to diet, physical activity, and other lifestyle and therapeutic interventions. Another analysis from the EPIC-Europe cohort showed a prospective association between physical activity levels and change in abdominal adiposity (waist circumference) independently of changes in BMI. In several lifestyle intervention trials, including the Hertfordshire Study, decreased waist circumference was an early indicator of success and improved cardiometabolic

risk profile among older adults who were involved in an endurance exercise program.

In summary, Prof. Wareham said that clinicians should select the best tools for measuring cardiometabolic risk that fit a specific purpose. That purpose may be to understand the etiology of disease, to predict disease in order to target therapy, to motivate individuals to change, or to be able to demonstrate response to lifestyle changes. Compared with BMI, measures of central obesity provide additional prognostic information and serve as more sensitive indicators of treatment response.

Abdominal Obesity Worsens Cardiometabolic Risk Profile Irrespective of BMI and Statin Treatment

Regardless of body mass index (BMI), patients with a higher accumulation of abdominal and liver fat have a worse cardiometabolic risk profile, according to new findings from the International Study of Prediction of Intra-Abdominal Adiposity and its Relationship with Cardiometabolic Risk/ Intra-Abdominal Adiposity (INSPIRE ME IAA).

Jean-Pierre Després, PhD, Université Laval, Quebec, Canada, presented results from three new INSPIRE ME IAA studies.

The INSPIRE ME IAA trial is an international imaging study that evaluated the relationship between abdominal obesity and cardiovascular disease (CVD) or type 2 diabetes. Beginning in 2006, the prospective trial enrolled 4277 patients across 29 countries and followed patients over a period of 3 years.

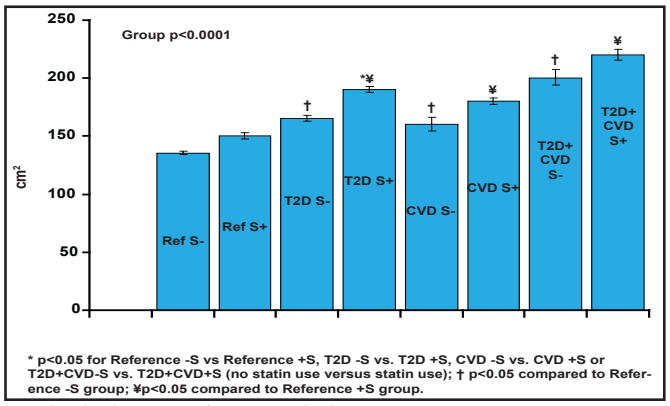
At baseline, 62% of patients had metabolic syndrome, 60% had hypertension, 39% had diabetes, and 24% had CVD. All patients underwent computed tomography (CT) imaging to measure subcutaneous and visceral adiposity and liver fat content. For both men and women, abdominal fat accumulation correlated significantly with liver fat content.

According to one INSPIRE ME IAA substudy, patients with prediabetes had significantly more visceral adipose tissue (VAT) and liver fat content than patients with normal glucose metabolism [Borel AL et al. Poster #329; Nazare JA et al. Poster #426]. Of several cardiometabolic risk factors, elevated liver fat accumulation was most closely associated with impaired glucose tolerance. Therefore, even before the onset of diabetes, abdominal obesity is an indicator of elevated cardiometabolic risk.

Another INSPIRE ME IAA substudy evaluated the relationships between body fat distribution and patient ethnicity [Smith JD et al. INSPIRE ME IAA Poster #215]. Across all ethnicities, higher BMI was correlated significantly with greater visceral fat accumulation and liver fat content. However, compared with other ethnicities, East Asian patients were more prone to gaining visceral adipose tissue as BMI values increased. This suggests that East Asian patients begin to accumulate visceral adipose tissue at lower BMI values, putting them at higher risk for diabetes and CVD than other patients with similar BMI levels. The emerging epidemic of obesity in Asia has especially dangerous implications for cardiovascular health in that part of the world.

INSPIRE ME IAA investigators also evaluated the potential role of statin therapy for managing cardiometabolic risk in patients with diabetes and/or CVD. Regardless of background pharmacotherapy, diabetes and CVD were associated with higher cardiometabolic risk. Total VAT and liver fat content was higher among patients with diabetes than without diabetes ($p<0.05$) and higher among patients with CVD than without CVD ($p<0.05$). In all disease categories, patients with a higher volume of VAT and liver fat content were more likely to be on statin therapy ($p<0.05$), suggesting that physicians recognized the worse cardiovascular risk profile in these patients and treated them more aggressively (Figure 1). Although statin therapy addresses some CVD risk factors, including elevated cholesterol, it does not effectively manage the residual cardiometabolic risk that is associated with abdominal obesity.

Figure 1. INSPIRE ME IAA: Visceral Adipose Tissue According to Statin Therapy, Type 2 Diabetes, and CVD.



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The INSIPRE ME IAA study may help to redefine our understanding of obesity, which is much more complex than having a high BMI, said Prof. Després. Irrespective of BMI, patients with excess abdominal fat have a worse cardiometabolic risk profile, even when managed with modern pharmacotherapy. Effective treatment may require interventions that address the specific metabolic risks that are associated with abdominal obesity.