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ADVANCED DIABETES

Evaluation and Management of Obesity in Diabetes

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Harvard Medical School

Osama Hamdy, MD, PhD; Sahar Ashrafzadeh, AB

Joslin Diabetes Center, Harvard Medical School,
One Joslin Place, Boston, MA 02215, USA

Osama Hamdy, MD, PhD

Dr. Osama Hamdy is a world expert and recognized thought leader in the area of obesity and nutrition in diabetes. Dr. Hamdy is a senior endocrinologist and medical director of the Joslin Obesity Clinical Program and director of the Inpatient Diabetes Program at Joslin Diabetes Center. He is also an associate professor of medicine at Harvard Medical School. In addition to his 34 years of extensive clinical experience, he is very active in nutrition and obesity clinical research. His lab led to many innovations and discoveries that changed how we currently manage obesity in patients with either type 2 or type 1 diabetes.

Dr. Hamdy's research led to the first discovery that seven percent weight loss in obese patients with and without diabetes significantly improved vascular endothelial function, insulin sensitivity, and markers of inflammation. This improvement may eventually prevent progression to coronary artery disease. Dr. Hamdy was a co-investigator in two landmark studies: the Diabetes Prevention Program and the Look AHEAD Study. In 2005, Dr. Hamdy founded the Weight Achievement and Intensive Treatment (Why WAIT) program, which is currently implemented nationally and internationally with great success. His program reduces total healthcare cost by an estimated 27 percent and diabetes-related cost by 44 percent and helps patients with diabetes to be less dependent on diabetes medications. Dr. Hamdy co-chaired the task force that developed the global transcultured Diabetes Nutrition Alogorithm (tDNA). His research led to several changes in the standards of diabetes care and lifestyle management by the American Diabetes Association and American Association of Clinical Endocrinologists.

Dr. Hamdy joined Joslin Diabetes Center in 1998, where he shared in developing the clinical research unit, founded the obesity clinical program, and restructured the inpatient diabetes program. At the inpatient side, he developed an Advanced Quality Improvement model for inpatient diabetes service that reduced 30-day readmission rates by 30 percent, and he also developed the EVADE program for management of Diabetic Ketoacidosis (DKA) in emergency departments that reduced ICU admission for DKA by 25 percent. Dr. Hamdy won the 2015 Michaela Modan Award of the American Diabetes Association for his research on long-term diabetes weight management. He was given the Compassionate Caregiver Award of the Kenneth Scwartz Center. Dr. Hamdy has authored more than 150 peer-reviewed original articles, reviews, and book chapters. He is also the author of the Harvard Health Publication *The Diabetes Breakthrough*, which outlines his strategy for long-term diabetes weight management. He is on the editorial review board of many medical journals including *Lancet, JAMA, British Medical Journal, and Diabetes Care*, and he is a two-time section editor of the *Current Diabetes Report*.

Outline/Table of Content

LEARNING OBJECTIVES

By the end of this chapter, learners will be able to:

- Examine the definition of obesity and its relation to type 2 diabetes
- Identify the pathophysiology of obesity in diabetes
- Design an effective weight management plan
- Recognize the results of intensive lifestyle interventions
- Discover digital health for diabetes and weight management

OVERVIEW

Introduction

A major health challenge in South Asians, which encompass residents of India, Pakistan, Bangladesh, Sri Lanka, Nepal, Bhutan, and Maldives, include type 2 diabetes (T2D) and obesity. Together, both diseases comprise what may be the largest epidemic in human history (1-3). These metabolic conditions are closely linked over 85% of individuals with T2D are either overweight or obese (4). The rise in obesity and T2D is a complex and multifaceted problem. Genetic, behavioural, social, and environmental attributes all contribute to an individual's risk of diabetes and obesity and recent studies have shown that epigenetics may also play a role in passing risk of T2D from one generation to the next (5, 6). Results from the INTERHEART study revealed that abdominal diabetes and obesity are among the nine easily measurable and modifiable risk factors that account for most of the risk for myocardial infarction in all regions of the world, irrespective of gender and age. Other risk factors include decreased physical activity; abnormal lipids; smoking; hypertension; psychosocial factors and decreased consumption of fruits; vegetables; and consumption of alcohol (7).

Globally, the prevalence of obesity is increasing rapidly, especially in India and other Asian countries. Several reasons are include an increase in energy intake owing to increased purchasing power, availability of high-fat, energy-dense foods; and a reduction in the energy expenditure consequent to urbanization and mechanization (21, 22). The change in food patterns has played an important role towards becoming overweight and obese, especially in children it has been reported that one in five children studying in schools of Delhi are obese or overweight (23). These overweight and obese children have a 70% risk of becoming overweight or obese adults.

Weight Management

Weight management is an effective method to help patients control their diabetes. According to clinical guidelines, lifestyle modification should be the first course of action in T2D management (8, 9). However, due to time and resource restraints, primary care physicians experience difficulty with effectively counseling patients on lifestyle behaviors, resulting in rapid initiation of diabetes pharmacotherapy (10-12). Unfortunately, many common medications used for diabetes treatment enhance weight gain (13). Weight gain results in increased insulin resistance (14), thus further driving the need for prescribing more antihyperglycemic medications or strengthening dosages of patients' existing medications to maintain glycemic control. Contrary to the patients' best interests, this practice leaves people with diabetes trapped in a viscous cycle.

Lifestyle Intervention

In contrast, implementing an intensive lifestyle intervention to help patients with T2D lose 7% of their body weight has been shown to enhance insulin sensitivity and to

improve glycemic control (15). To encourage patients to maintain lifestyle interventions, an initial goal would be to achieve a sustainable weight loss of 0.5 kg per week for those who are overweight (16). The Diabetes Prevention Program (DPP), an intervention similarly aimed to help individuals with prediabetes and obesity lose 7% of their body weight, demonstrated that weight loss reduced the incidence of T2D by 58% after approximately three years when compared to patients who did not participate in the DPP weight loss program (17); weight loss during the first two years was the strongest predictor of reduced diabetes risk and improvement in fasting plasma glucose (18). Furthermore, the Action for Health in Diabetes (Look AHEAD) study showed that lifestyle modification among individuals with T2D led to better glycemic control and weight loss among patients (19). Participants in the intensive lifestyle intervention also reduced their use of medications for hypertension, dyslipidemia, and diabetes had reduced risk of depression and chronic kidney disease; and experienced fewer hospitalizations in comparison to participants in the control group, who underwent diabetes support and education only (19).

Maintaining Weight Loss

While weight management effectively helps patients control T2D, an important challenge remains: how can we help patients maintain their weight loss for years to come? A recent study reported that patients with diabetes and obesity who participated in an intensive lifestyle intervention program were able to sustain weight loss for five years in real-world clinical practice (20). Using a multidisciplinary approach to lifestyle management is key to helping patients with T2D achieve long-term weight loss in real-world clinical practice, as will be further explained in this chapter.

Strategies for Weight Loss

When discussing strategies for weight loss with a patient and/or their caregiver(s), the following steps are recommended for setting behavioral goals and objectives, with a focus on developing specific objectives and then letting the patient take the lead. The patient's healthcare provider can assist in keeping behavioral objectives FIRM (24).

- **F**ew in number. Keep the number of changes to a minimum (e.g., one goal aimed at increasing physical activity); this can increase likelihood of success.
- **I**ndividualized objectives, tailored to the patient and their lifestyle, income, habits, and likes/dislikes.
- **R**ealistic. Help the patient to choose practical, attainable goals (e.g., switching from regular to diet soda). Even small changes can result in greater initial success for overall weight loss, which can have a significant impact on health. Oftentimes, patients believe they have to achieve a normal body weight within a specific time frame, but improvements can be achieved with initial weight losses of 0.5 kg/week.

- **M**easurable. Set specific metrics, such as walking 3,000 steps a day by using a pedometer for 2 weeks, then 5,000 steps a day for a week, then 7,000 steps a day for a week, with an overall goal of 10,000 steps a day.

Counseling Patients

When counseling (assessing) a patient, it is important to have a conversation about their weight and a weight management strategy, to discuss lifestyle modifications and to try to refer the patient to another resource for more information (25). Recommendations when counseling include:

- Finding out what a patient already knows about their condition before providing information. Many times, other members of the healthcare team have discussed information with the patient, which can have the effect of coloring patient perceptions and perhaps even causing confusion when new information is introduced. However, not all patients want the same level of detail in the information offered about their condition or treatment. Evidence has shown that patients are on a continuum of information-seeking from those who want very little information to those who want every detail the physician can offer. Thus, practitioners should assess (ask) whether the patient desires, or will be able to comprehend, additional information.
- Determine what is of concern/importance to the patient.
- Avoid engaging in long monologues with the patient/their caregiver(s). Keep statements short, with clear, simple explanations. Tailoring information to a patient's desired level of information will improve comprehension and limit emotional distress.

Referring Patients

Clinicians also need to know when to refer patients, whether to other members of the healthcare team to support and enhance the management strategy, or simply for more information, such as community programs, specific websites, and various tools to help the patient succeed. Management strategies work best when the patient, their caregiver(s), and the healthcare provider meet on common ground to assess a problem, set behavioral change goals, monitor progress, and provide follow-up. The key is to get to AGREE:

- **A**ssess (their current lifestyle)
- **G**enerate (treatment plan goals to which the patient agrees)
- **R**ecord progress (provide a diary, log, or smartphone application to monitor their food intake and physical activity)
- **E**valuate (at each visit their progress for each goal)
- **E**mpower (patients succeed when they feel empowered) (26). And once certain goals are met and evaluations are complete, reassess with the patient to create new goals to accomplish.

OBESITY RISK FACTOR FOR T2D

Evaluation of Obesity

Nutritional status assessments should be performed for each patient, ideally by a registered dietitian nutritionist (RDN) or by physician who is familiar with obesity management (27). If an RDN is not available, a teleconsultation can be conducted between the patient and an offsite RDN if possible, or a member of the clinic staff may be trained to assess nutritional status of patients. A complete history and a thorough evaluation are needed to help determine the underlying causes of obesity and to establish a treatment plan (28).

Body Mass Index

Overweight and obesity are assessed and diagnosed by body mass index (BMI) after measuring both height and weight

$$\text{BMI} = \frac{\text{Weight (kg)}}{[\text{Height (m)}]^2}$$

A patient who presents with BMI of 25–29.9 kg/m^2 (23–27 kg/m^2 in patients of Asian ethnicity) is considered overweight, and a patient with BMI ≥30 kg/m^2 (≥27 kg/m^2 in Asian population) is considered obese (29).

Achieving a lower BMI can have beneficial effects on survival. Results from a collaborative analysis of baseline BMI versus mortality from 57 prospective studies showed for those who would reach a BMI of 25–27.5 kg/m^2 by approximately 60 years of age, their median survival decreased by up to 12 months; for those who would reach a BMI of 27.5–30 kg/m^2, median survival decreased by 1–2 years and for those who would become obese (BMI of 30–35 kg/m^2), median survival decreased by 2–4 years (30). For those with a BMI >35 kg/m^2, less data was available, although for those who would become morbidly obese (BMI of 40–50 kg/m^2), median survival appears to decrease by approximately 8–10 years.

Measuring Adiposity

However, BMI is a crude measure of adiposity as it does not differentiate between lean body mass and body fat mass. Hence, the assessment for excess adiposity should be performed after considering muscularity, sarcopenia, and hydration status (31). Further assessments of waist circumference should be conducted for patients with a BMI ≥25 kg/m^2 but <35 kg/m^2 (29). Because waist measurement is more prone to errors than measuring height and weight, it is recommended to use all three. But it is essential that healthcare practitioners, technicians, and patients use appropriate techniques for measuring waist circumference so reliable data can be obtained.

Measurements should be made around a patient's bare midriff, after the patient exhales while standing without shoes, both feet touching, and arms hanging freely. The

measuring tape should be made of a material that is not easily stretched, such as fiberglass. The tape should be placed perpendicular to the long axis of the body and horizontal to the floor and applied with sufficient tension to conform to the measurement surface. Although not normally performed in the office, waist circumference measurements are typically taken three times and recorded to the nearest 0.1 cm in a research setting. Despite specific techniques being recommended for measuring waist circumference in the clinical setting, there is no uniformly accepted approach (32).

In the United States, waist circumference ≥88cm (35 inches) in women and ≥102 cm (40 inches) in men indicates abdominal adiposity and increased risk for the cardio metabolic disease. The International Diabetes Federation recommends ethnic-specific values for determining cutoffs for waist circumference of different ethnicities, such as South Asians, Japanese, and Chinese (33). Among patients of Asian ethnicities, waist circumference ≥80 cm higher risk (29).

Approximately 85% of total adipose tissue mass is located under the skin (subcutaneous fat), with the remainder, approximately 15%, being located within the abdomen (intra-abdominal fat). The relative contribution of intra-abdominal fat mass to total body fat is influenced by sex, age, race/ethnicity, physical activity, and total adiposity. The term "visceral fat" is commonly used to describe intra-abdominal fat and includes both intraperitoneal fat (mesenteric and omental fat), which drains directly into the portal circulation, and retroperitoneal fat, which drains into the systemic circulation.

Visceral Fat

Excess fat within the abdomen and other organs, as opposed to subcutaneous tissues, is a more potent risk factor than BMI, and has been linked with glucose intolerance, dyslipidemia, and hypertension, as well as insulin resistance (34). Visceral fat is more insulin resistant and more metabolically active than subcutaneous fat and has been shown to release excess toxic cytokines, proinflammatory molecules, and vasoactive hormones, as well as driving excess free fatty acids and cortisol directly to the liver. This excess visceral fat is more metabolically active than subcutaneous fat, has greater endocrine activity, and causes greater adverse effect on metabolism and CV risk (35). One study showed among overweight/moderately obese men and women, after adjusting for BMI, increases in visceral adipose tissue increased the risk for insulin resistance, whereas increases in subcutaneous adipose tissue decreased the risk for insulin resistance (36).

As a result of increased visceral fat, the relationship between waist circumference and clinical outcomes is consistently strong for diabetes risk, and waist circumference is a stronger predictor of diabetes than is BMI. However, American College of Cardiology (ACC)/American Heart Association (AHA)/The Obesity Society (TOS) guidelines on obesity note that is not necessary to measure waist circumference in patients with BMI

>35, as this measurement will likely be elevated and it adds no additional risk information (32).

Waist to Height Ratio (WHtR)

Along with BMI and waist circumference, waist-to-height ratio (WHtR), also referred to as the Index of Central Obesity, has been confirmed as an index in both adults and children for identifying those at increased risk of cardiometabolic disease (37–39). The calculation takes into account the individual's height, which is important particularly in shorter individuals and those of various ethnicities. A 10 cm increase in waist circumference and WHtR of >0.5 were associated with a significant increase in risk for developing T2D in several countries around the globe, from a 26% increase in India, to a 60% increase in China and Spain, and a 77% increase in Finland (40). Thus, a proposed single value of <0.5 is recommended as a cutoff for increased cardiometabolic risk, whether male or female, adult or child, irrespective of ethnicity (41).

Several other studies support this conclusion. Kodama et al. reported that a WHtR had a stronger association with diabetes incidence than BMI and WHR (42). Ashwell et al. revealed WHtR was better than BMI and waist circumference in determining cardiometabolic risk (43). Lyssenko et al. showed WHtR was a risk factor that increased the risk by 2.3-fold ($p < .001$) for predicting T2D (44). In a meta-analysis by Savva et al., the overall ratio of relative risks detecting T2D clearly indicated WHtR is superior to BMI (45). And in a study of Asian Indians in northern India with high prevalence of cardiometabolic risk factors, a combination of waist circumference and WHtR appeared to have better clinical utility than BMI and waist-to-hip in identifying individuals with cardiometabolic risk factors (46).

Regarding ethnicity, the association of WHtR with T2D is stronger in both Asians and non-Asians, whether male or female (47). Because of this, it is recommended WHtR be included in the routine screening and assessment of overweight and obese individuals, especially children (48). Those with an elevated WHtR should undergo a further assessment for cardiometabolic risk.

Co-morbidites

Besides BMI and waist circumference, recommendations suggest evaluating other comorbidities commonly associated with adiposities, such as sleep apnea and non-alcoholic fatty liver diseases (29, 31). In addition, individual eating pattern, nutritional needs, nutritional status, weight history, and previous exposure to nutrition education are required before recommending a nutrition therapy plan (28).

Weight History

Taking an accurate weight history can help to determine the potential for increased risk. For example, individuals who were once obese but then achieved a normal weight had an almost doubled risk of a CV event (HR of 1.80; 95% CI, 1.23–2.64) compared with individuals who maintained a normal-weight category the whole time. In an

analysis of 6,197 participants from the original and offspring Framingham Heart Study, the mortality rate for overweight individuals were 47.48 per 1000 person-years and for obese individuals, 66.67 per 1000 person-years (49). Meanwhile, people who never exceeded normal weight (BMI 18.5–24.9) had a mortality rate of 27.93 per 1000 person-years (49).