AMERICAN DIABETES ASSOCIATION-SELF-ASSESSMENT PROGRAM:
CARDIOMETABOLIC RISK

Target Audience
All health care professionals involved in treating individuals with, or at risk for, diabetes, including physicians, physician assistants, nurses, nurse practitioners, dietitians, pharmacists, and other health care professionals.

Learning Objectives
I. Identify cardiometabolic risk (CMR) factors associated with the pathophysiology of cardiovascular (CV) disease in persons with, or at risk for, prediabetes or type 2 diabetes.
II. Implement screening strategies for individuals with CMR into clinical practice to promote early detection and prevention of prediabetes or diabetes.
III. Discuss how preventing CMR factors can positively impact CV health in persons with, or at risk for, prediabetes or type 2 diabetes.
IV. List treatment options and define goals of treatment directed toward CMR factors.
V. Incorporate into clinical practice evidence-based data from clinical trials and recommendations from clinical practice guidelines toward the optimal management of individuals with CMR.

Abbreviations used throughout this program:
A1c=glycosylated hemoglobin A1c
ACC=American College of Cardiology
ACCOMPLISH=Avoiding Cardiovascular Events in Combination Therapy in Patients Living with Systolic Hypertension
ACCORD=Action to Control Cardiovascular Risk in Diabetes
ACE=angiotensin converting enzyme
AHA=American Heart Association
AHEAD=Action for Health in Diabetes
ARB=angiotensin receptor blocker
Association=American Diabetes Association
ATP-III=Adult Treatment Panel
BMI=body mass index
BP=blood pressure
CMR=cardiometabolic risk
CABG=coronary arterial bypass graft
CRP=c-reactive protein
CV=cardiovascular
DASH=Dietary Approaches to Stop Hypertension
DBP=diastolic blood pressure
DPP=Diabetes Prevention Program
DSME= diabetes self-management education
DSMS=diabetes self-management support
DSE=diabetes support education
FDA=Food and Drug Administration
FPG=fasting plasma glucose
GDM=gestational diabetes mellitus
HDL-C=high-density lipoprotein cholesterol
IFG=impaired fasting glucose
IGT=impaired glucose tolerance
INSPIRE ME IAA=International Study of the Prediction of Intra-Abdominal Adiposity and its Relationship with CMR/Intra-Abdominal Adiposity
ILI=intensive lifestyle intervention
IPG=impaired fasting glucose
LDL-C=low-density lipoprotein cholesterol
NHANES=National Health and Nutrition Examination Survey
OHS=obesity-hypoventilation syndrome
OGTT=oral glucose tolerance test
OmniHeart=Optimal Macronutrient Intake Trial for Heart Health
OSA=obstructive sleep apnea
PCI=percutaneous coronary intervention
PTDS=post-traumatic stress disorder
REMS= risk evaluation and mitigation strategy
SBP=systolic blood pressure
SSB=sugar-sweetened beverages
TZD=thiazolidinedione
TOS=The Obesity Society
U.S.=United States
VLDL=very low-density lipoprotein cholesterol

WHR=waist-to-hip ratio

WHtR=waist-to-height ratio
CASE STUDY #1

HT, a 39-year old Japanese-American male, comes in for a routine check-up. In reviewing his medical record, you note that he has had difficulty controlling his blood glucose over the past 20 years, with FPG levels fluctuating between 95 mg/dL and 115 mg/dL. Over that time period, you have consistently counseled him to increase his level of exercise, but his work schedule was so erratic that he did not. In addition, his occupation (actor) required him to intermittently add excessive weight (30-40 pounds) and then is forced to lose that weight in a short amount of time.

Physical exam: height, 5’10” (177.8 cm); weight, 180 lbs (84 kg); BMI, 25.8 kg/m²; waist circumference, 38 inches (96.5 cm); SBP, 126 mmHg; DBP, 80 mmHg (average of 3 readings).

Social history: 1-2 glasses of wine a day; denies tobacco use; no structured exercise program, although his work does involve physical activity at times.

Lab results (within the past week): A1c, 6.0%; fasting blood glucose, 108 mg/dL; total cholesterol, 190 mg/dL; LDL-C, 124mg/dL; HDL-C, 34 mg/dL; triglycerides, 160 mg/dL.

Medications: None

Assessment: HT has prediabetes, but is otherwise is healthy and in no acute distress.

Questions 1-15

1. IFG is a condition in which the FPG level is between:

A. 75 and 100 mg/dL  
B. 100 and 125 mg/dL  
C. 125 and 150 mg/dL  
D. 140 and 199 mg/dL  
E. >200 mg/dL

Answer: B

Rationale:

Individuals with IFG and/or IGT have been referred to as having prediabetes, indicating the relatively high risk for the future development of diabetes. By definition, IFG is a condition in which FPG levels range between 100 mg/dL (5.6 mmol/L) and 125 mg/dL (6.9 mmol/L) after an 8 to 12 hour fast. IGT is defined as having 2-hour plasma glucose values from an OGTT of 140 mg/dL (7.8 mmol/L) to 199 mg/dL (11.0 mmol/L). If the 2-hour blood glucose rises to 200 mg/dl or above, a person has diabetes.

For A1c, clinical research studies that used this measurement to predict the progression to diabetes demonstrated a strong, continuous association between A1c and subsequent diabetes. An A1c range of 6.0–6.5% had a 5-year risk of developing diabetes between 25 to 50%, with a relative risk 20 times higher compared with an A1c of 5.0%. Other analyses suggest that an A1c of 5.7% is associated with diabetes risk similar to that in the high-risk participants in the Diabetes Prevention Program (DPP). The American Diabetes Association’s Standards of Care state that it is reasonable to consider an A1c range of 5.7–6.4% as identifying individuals with prediabetes. Thus, HT’s A1c of 6.3% meets the criteria for prediabetes.

Reference(s):


2. **Prediabetes is a state in which:**

A. One’s blood glucose level falls within the normal range.
B. A patient has IFG and/or IGT.
C. One’s blood glucose level is higher than normal, but not yet high enough to be diagnostic of diabetes.
D. Both b and c
E. All of the above

**Answer:** D

**Rationale:**

Recognizing clinical signs in individuals at risk for developing diabetes is a key to prevention. Two signs that should alert clinicians are higher than normal blood glucose levels, based upon IFG, IGT, and/or an elevated A1c level. Although these levels may not high enough to be classified as diabetes, many clinicians disregard their significance. IFG and IGT should be viewed as risk factors for diabetes as well as CV disease rather than clinical entities, as they are associated with obesity (especially abdominal or visceral obesity), atherogenic dyslipidemia with high triglycerides and/or low HDL-C, and hypertension. Thus, there is a relatively high risk for the future development of diabetes for individuals with IFG, IGT, and/or elevated A1c despite not having diabetes by a clinical definition. This condition is called prediabetes.

**Reference(s):**


3. **Insulin resistance is a key feature in type 2 diabetes, as well as:**

A. Dyslipidemia
B. Endothelial dysfunction
C. Obesity
D. Acanthosis nigricans  
E. All of the above  

Answer: E  

Rationale:  
Insulin resistance is characterized by the impaired function of insulin to stimulate glucose disposal in peripheral tissues and suppress hepatic glucose production. Insulin resistance is a key feature of type 2 diabetes, as well as dyslipidemia, obesity, hypertension, and endothelial dysfunction.  

Reference(s):  

4. Which of the following statement(s) are true?  
A. CV disease risk escalates with increasing hyperglycemia and insulin resistance, which may occur long before the clinical diagnosis of diabetes.  
B. IFG confers a much greater risk of coronary heart disease, CV disease, and overall mortality than the presence of the metabolic syndrome.  
C. CMR only includes the major components of the metabolic syndrome and no other factors that affect risk, such as lifestyle and genetic factors.  
D. A and B above.  
E. A and C above.  

Answer: A  

Rationale:  
CMR is preferred term to denote both the cluster of risk factors traditionally known as metabolic syndrome, which includes traditional parameters of CV disease risk (waist circumference, triglycerides, HDL-C, blood pressure, IFG), as well as risk markers resulting from abdominal obesity (certain cytokines and adipokines). The term captures all risk related to the metabolic changes associated with CV disease and not just those fitting the metabolic syndrome definition. CV risk factors, such as hypertension, diabetes, elevated cholesterol and atherogenic dyslipidemia, and cigarette smoking promote oxidative stress to cause endothelial dysfunction, initiating a cascade of events. These events include alterations in vasoactive mediators, inflammatory responses, and vascular remodeling, which culminate in target-organ damage. Evidence indicates that these processes begin earlier in life than previously recognized, indicating that CV disease occurs over decades, long before the clinical diagnosis of diabetes.  

Reference(s):  

5. The most common cause of acquired insulin resistance is:

A. BMI <23 kg/m² without abdominal obesity
B. Abdominal (visceral) obesity
C. Increased subcutaneous fat deposition
D. CRP level <1.0 mg/L
E. FPG level <100 mg/dL

**Answer: B**

**Rationale:**

An important component of increased CMR is abdominal obesity (increased waist circumference), and is caused by excess abdominal visceral fat. 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.

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. Visceral fat also has a greater ability to release cytokines and adipokines than subcutaneous fat. These cytokines and adipokines have an impact on causing insulin resistance, elevating triglyceride and small-dense LDL-C levels, hyperinsulinemia, and endothelial dysfunction, all of which can contribute to vascular damage. 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.

A BMI of <25 kg/m² is considered to be an optimal weight and not considered to be the most common cause of insulin resistance, especially in the absence of abdominal obesity. CRP is a measurement of inflammation and used to further evaluate underlying risk, but not a cause of insulin resistance. An individual with a high-sensitivity-CRP level of <1.0 mg/L is considered at low risk.

**Reference(s):**


6. Excess fat within in the abdomen (visceral adiposity) is:

A. A traditional marker for CV disease risk  
B. More strongly associated with CMR than overall weight or BMI  
C. A less potent risk factor than BMI  
D. Is less metabolically active than subcutaneous fat  
E. A surrogate measure of increased insulin sensitivity

Answer: B

Rationale:
CMR comprises a cluster of risk factors that are good indicators of an individual’s overall risk for CV disease and type 2 diabetes. CMR also includes visceral obesity and other markers not traditionally considered in CV disease risk assessment. A more potent risk factor than BMI, excess fat within the abdomen and other organs, as opposed to subcutaneous tissues, has been linked with glucose intolerance, dyslipidemia, and hypertension, as well as insulin resistance. 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.

Reference(s):

Answer: B

Rationale:

BMI is an index of general adiposity. Because waist measurement is more prone to errors than measuring height and weight, it is recommended to use all three. BMI best illustrates an estimate of the level of obesity, while waist measurement gives an estimate of visceral fat and risk of obesity-related diseases, such as diabetes. 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. But, waist circumference can identify persons who are at greater CMR than those identified by BMI alone. Beyond waist circumference, the waist-to-hip ratio is used to determine the severity of central obesity. Although total cholesterol/HDL-C ratio is used as a marker for increased insulin resistance, it is not a marker of visceral obesity.

The most recent ACC/AHA/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. As an indication of increased CMR, these guidelines continue to recommend using the current cutpoints: >35 inches (88 cm) for women and >40 inches (102 cm) for men. Thus, a large waist circumference is a key surrogate measure of insulin resistance when assessing risk of incident diabetes and CV disease.

Reference(s):


8. Based upon results from the from the International Study of the INSPIRE ME IAA study, what was the impact of diabetes treatment for achieving the American Diabetes Association's (Association's) goals for HDL-C or triglycerides despite the presence of excess visceral adipose tissue and liver fat?

A. Fewer patients with excess visceral adipose tissue or liver fat achieved the Association’s goals for the two lipid parameters compared to patients with low visceral adipose tissue or liver fat regardless of diabetes treatment.
B. More patients with excess visceral adipose tissue or liver fat achieved the Association’s goals for the two lipid parameters compared to patients with low visceral adipose tissue or liver fat.
C. Fewer patients with excess visceral adipose tissue or liver fat achieved the Association’s goals for HDL-C but not triglycerides compared to patients with low visceral adipose tissue or liver fat.
D. Fewer patients with excess visceral adipose tissue or liver fat achieved the Association’s goals for triglycerides but not HDL-C compared to patients with low visceral adipose tissue or liver fat.
E. None of the above

Answer: A

Rationale:
Both visceral adipose tissue and liver fat are strongly associated with insulin resistance and type 2 diabetes. In a cross-sectional analysis of baseline data (N = 3991) from the INSPIRE ME IAA study, patients were divided into four groups: those without type 2 diabetes (n=1003 men, n=1027 women); those with type 2 diabetes but not treated with diabetes medications (n=248 men, n=198 women); those with type 2 diabetes and treated with diabetes medications but not yet using insulin (n=591 men, n=484 women), and those with type 2 diabetes and treated with insulin (n=233 men, n=207 women).

Results showed fewer patients with excess visceral adipose tissue or liver fat achieved the Association’s goals for HDL-C or triglycerides compared to patients with low visceral adipose tissue or liver fat. Both visceral adiposity (p = .02 men, p = .003 women) and liver fat (p = .0002 men, p = .0004 women) were increased among patients who met fewer of the Association treatment criteria, regardless of type 2 diabetes treatment. Residual CMR exists among patients with type 2 diabetes characterized by elevated VAT and LF.

Reference(s):

9. Which of the following is INCORRECT regarding how to measure waist circumference?

A. There is a uniformly-accepted approach when measuring waist circumference.
B. Measurement should be made around an individuals’ bare midriff, after they exhale while standing without shoes, both feet touching, and arms hanging freely.
C. The measuring tape should be made of a material that is not easily stretched.
D. 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.
E. All of the above.

Answer: A

Rationale:
Waist circumference 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. And although specific techniques have been recommended for measuring waist circumference in the clinical setting, there is no uniformly accepted approach. However, it is essential that both healthcare practitioners, technicians, and patients use appropriate techniques for measuring waist circumference, so reliable data can be obtained.

**Reference(s):**


10. HT has a waist circumference of 38 inches. For a male, this measurement is less than the guidelines cite as having an increased CMR due to abdominal obesity. What would be a more accurate measure to determine an increased risk from abdominal obesity?

A. BMI  
B. Waist-to-hip ratio  
C. Waist-to-height ratio (index of central obesity)  
D. Total cholesterol/HDL-C ratio  
E. None of the above  

Answer: C

**Rationale:**  
Along with BMI, waist circumference and WHR are also associated with increased CMR and risk of death. However, the WHtR (also referred to as the Index of Central Obesity) has emerged as a promising index for identification of subjects at increased CMR in both adults and children, as the calculation takes into account height, which is important particularly in shorter individuals and those of various ethnicities. A proposed single value of <0.5 is recommend as a cutoff for increased risk, whether male or female, adult or child, irrespective of ethnicity. Several studies support this conclusion.

Kodama et al showed that WHtR had a stronger association with incident diabetes than BMI and WHR. Ashwell et al showed that WHtR had a better discriminatory power than BMI and WC in detecting several CMR factors. And in a meta-analysis by Savva et al, the overall ratio of relative risks clearly indicated WHtR is superior to BMI in detecting type 2 diabetes. Regarding ethnicity, the association of WHtR with type 2 diabetes was stronger in both Asians and non-Asians, whether male or female. Because of this, it is recommended WHtR be included in the routine screening and assessment of overweight and obese children, and those with an elevated WHtR should undergo a further CMR assessment.

With a WHtR of 0.54, HT is at increased CMR, despite having a waist circumference less than that defined by the guidelines as a measure of increased CMR.

**Reference(s):**


11. Based upon clinical evidence, each of the following race/ethnicities may require a lower cutoff level for waist circumference EXCEPT:

A. African American  
B. Japanese  
C. Caucasian  
D. South Asians  
E. Hispanic Americans

**Answer:** C
**Rationale:**

In various guidelines and the Association’s Standards of Care, cutoff values for waist circumference (≥40 inches for men; ≥35 inches for women) were derived from values that correlated with a BMI ≥30 kg/m². The International Diabetes Federation recommends ethnic-specific values for determining cutoffs for waist circumference of different ethnicities, such as South Asians, Japanese, and Chinese. Accordingly, certain races/ethnicities in the U.S. may require a lower cutoff, including African Americans, Hispanic Americans, South Asians, Chinese, and Japanese because of a greater risk for developing CMR.

**Reference(s):**


**Case 1 Continuation**

12. You discuss with HT some treatment options, including increasing his physical activity, intensity of exercise, weight management, and diet. In a person with prediabetes, weight management and routine exercise:

A. Are seldom advised for patients with clear CMR
B. Can delay or prevent the onset of diabetes
C. Improve risk factors for CV disease
D. Both b and c
E. All of the above

**Answer:** D

**Rationale:**

Persons with prediabetes, including those with regular access to health care, might benefit from educational efforts aimed at increasing awareness that they are at risk for developing type 2 diabetes, as
they can reduce that risk by making modest lifestyle changes. Evidence-based lifestyle programs that encouraged dietary changes, moderate-intensity physical activity, and modest weight loss for persons diet with prediabetes have shown a delay or prevention of type 2 diabetes. Exploratory analysis from the Look AHEAD study results showed ILI was associated with a greater likelihood of partial remission of type 2 diabetes compared with DSE. In the DPP, the incidence of type 2 diabetes in persons at high risk was reduced by 58% in the lifestyle intervention group and 31% in the metformin group, as compared with placebo; the lifestyle intervention was significantly more effective than metformin.

Reference(s):


13. The American Diabetes Association recommends a structured program that emphasizes lifestyle changes for individuals at high risk for developing type 2 diabetes. This type of program includes which of the following:

A. Regular physical activity of less than 90 minutes per week.
B. Moderate physical activity of at least 150 minutes per week.
C. Dietary strategies that include only a reduction in calories to achieve a targeted body weight loss of 3%.
D. Dietary strategies that include both a reduction in calories and reduced intake of dietary fat to achieve a targeted body weight loss of 7%.
E. B and D above

Answer: E

Rationale:

Evidence-based lifestyle programs that encouraged dietary changes, moderate-intensity physical activity, and modest weight loss for persons with prediabetes have shown a delay or prevention in the onset of type 2 diabetes. The Association recommends structured programs that emphasize lifestyle changes for individuals at high risk for developing type 2 diabetes. These programs should include moderate physical activity of 150 min per week or intense physical activity of 90 minutes per week, and dietary strategies (reduced calories and reduced intake of dietary fat) in order to achieve a targeted body weight loss of 7%.

Reference(s):


Case 1 Continuation

It is important that HT is exercising, but he is only maintaining his weight, not losing nor gaining. And his latest A1c is 6.3%. He asks what more can be done to reverse his prediabetes and prevent type 2 diabetes.

14. As noted, exercise and weight reduction are important for preventing type 2 diabetes. What percent of individuals with prediabetes who do not lose weight and/or do not engage in moderate physical activity will progress to type 2 diabetes during the average 3 years of follow-up?

A. 1%
B. 4%
C. 11%
D. 17%
E. 21%

Answer: C

Rationale:
There is a relatively high risk for the future development of diabetes for individuals with IFG, IGT, and/or elevated A1c despite not having diabetes by a clinical definition, a condition called prediabetes. In 2010, approximately one in three U.S. adults aged ≥20 years (an estimated 79 million persons) had prediabetes. Of these, only 11% of persons with prediabetes were aware that they had the condition. And each year approximately 11% of persons with prediabetes who do not lose weight and/or do not engage in moderate physical activity will progress to type 2 diabetes.

Reference(s):


15. In addition to exercise as a cornerstone therapy for diabetes prevention, the Association’s Standards of Care recommends healthcare practitioners consider which of the following for individuals with IFG, IGT, and an A1c of 5.7–6.4%?

A. Sulfonylurea
B. DPP-4 antagonist
C. Metformin
D. GLP-1 receptor agonist
E. Alpha-glucosidase inhibitor

Answer: C

Rationale:
Metformin has been shown to activate the key regulatory enzymes that may prevent the transition from prediabetes to type 2 diabetes. In one study, insulin sensitivity was considerably higher after 12 weeks of exercise training and/or metformin for individuals with prediabetes. Other evidence showed a greater weight loss (2-5 kg) occurred with the addition of metformin compared with lifestyle modification alone. The DPP also demonstrated that either lifestyle modification (i.e., low-fat diet and increased physical activity) or metformin can reduce the transition from prediabetes to type 2 diabetes.

In addition to exercise as a cornerstone therapy for diabetes prevention, the Association’s Standards of Care also recommends healthcare practitioners consider metformin therapy for individuals with IGT, IFG, or an A1c of 5.7–6.4%, especially for those with BMI $\geq$35 kg/m$^2$, aged 60 years or older, and women with prior GDM.

Reference(s):


Case Study #2

FD, a 68-year-old African American male, comes in for a routine clinic visit. He was diagnosed with essential hypertension 8 years ago with a SBP, 146 mmHg; DBP, 98 mmHg; currently, his BP is controlled on medication.

Social history: 40-year history as a 1 pack-per-day smoker; no family history of premature coronary disease. Was a business executive in the pharmaceutical industry; he is currently employed as a consultant in healthcare. Physical activity is limited to 20 minutes per day of walking to and from work. Diet is erratic, frequently dining out with clients, including 2-3 glasses of wine a day.

Physical examination: SBP/DPB, 138/87 mmHg (average of 3 readings); body mass index (BMI), 31 kg/m²; waist circumference, 42 inches (102.9 cm).

Recent lab data: fasting lipid panel is notable for total cholesterol, 218 mg/dL; LDL-C, 144 mg/dL; HDL-C, 29 mg/dL; triglycerides, 226 mg/dL; FPG, 115 mg/dL.

Medications: amlodipine 5 mg once daily.

Assessment: FD is an obese African American with essential hypertension, dyslipidemia, and several factors contributing to CMR.

Questions 16-35

16. Which of the following are modifiable CMR factors?

A. Race/ethnicity
B. Family history
C. Hypertension
D. Age
E. Gender

Answer: C

Rationale:

CV disease is the leading cause of death in the U.S. and many parts of the world. Modifiable CV and CMR factors include obesity, tobacco use, physical inactivity, unhealthy diet, hypertension, abnormal lipid metabolism (e.g. elevated LDL-C), as well as a cluster of interrelated metabolic risk factors, such as inflammation/hypercoagulation and insulin resistance.

FD has a total of 7 modifiable CMR factors. Of those listed above, he has hypertension; family history, racial/ethnicity, gender, and age are non-modifiable. His other modifiable CMR factors include physically inactive (walks only 20 minutes per day), being overweight, has dyslipidemia, smokes, eats an unhealthy diet, and is insulin resistant. He probably has some level of vascular inflammation based upon his an elevated triglyceride/HDL-C ratio (indicating insulin resistance), but a CRP level would help to determine the presence of that risk factor.

Reference(s):


17. Each of the following statements is correct regarding CMR in different ethnicities EXCEPT:

A. CV disease, diabetes and related risk factors occur at higher rates among certain racial and ethnic groups, including African Americans and Hispanic Americans.

B. African American men and women have the highest age-adjusted prevalence of high blood pressure.

C. African American women have the highest age-adjusted prevalence of abdominal obesity.

D. Conventional risk criteria does not need to be adjusted to accommodate for differences across ethnic groups and, in turn, gain a more accurate assessment of CMR and existing disease.

E. Death rates from heart disease are higher among adults that are African American than Caucasians.

**Answer: D**

**Rationale:**

The prevalence, impact, and control of diabetes and CV disease differ across racial and ethnic subgroups of the U.S. population. For example, in African Americans, hypertension is more common, more severe, and develops at an earlier age. This group also has a greater prevalence of other risk factors, especially obesity. However, much of the disparity among ethnic groups may be attributable to differences in socioeconomic condition, access to health care, or attitudes toward health-related information.

Demographic factors also influence the likelihood of other risk factors for type 2 diabetes and CV disease. Overweight and obesity correlate with a higher incidence of type 2 diabetes, hypertension, and heart disease. Hispanics, Native Americans, and African Americans are all more likely than Caucasians to be overweight or obese, even as children, so their overall risk as demographic groups for developing diabetes and/or CV disease is greater than that of the Caucasian population.

**Reference(s):**


18. Which of the following statements is CORRECT regarding CMR?

A. Only pharmacologic interventions have been proven to benefit patients with CMR.
B. Treatment goals for patients with CMR include achieving targets for blood glucose, blood pressure, and dyslipidemia.
C. All patients with elevated high-density lipoprotein cholesterol need to be treated aggressively with lifestyle modifications and adjunctive drug therapies.
D. Research results are inconclusive in the need for primary prevention of obesity beginning in childhood.
E. The risk of myocardial infarction, strokes, and CV death is not increased.

Answer: B

Rationale:
The primary treatment of elevated CMR is lifestyle modification, as it has been shown to provide benefit in patients with CMR. In addition to glycemic control, both national and international guidelines on management of diabetes emphasize control of blood pressure, dyslipidemia, and obesity. The INTERHEART study revealed nine easily measurable and modifiable risk factors (abnormal lipids; smoking; hypertension; diabetes; abdominal obesity; psychosocial factors; decreased consumption of fruits, vegetables, and alcohol; decreased physical activity) account for most of the risk for myocardial infarction in all regions of the world, irrespective of gender and age. For individuals with CMR, the risk of myocardial infarction, strokes, and CV death is 13 times higher than for those without CMR.

Reference(s):


19. Which factor(s) play(s) a clear role in increasing a person’s CMR, but are not included in the traditional classification of metabolic syndrome?

A. HDL-C levels
B. Tobacco use
C. Hypertension
D. Waist circumference
E. All of the above

Answer: B

Rationale:
There are many individuals who have a constellation of major risk factors, life-habit risk factors, and emerging risk factors that constitute a condition called the metabolic syndrome. Factors characteristic of
The term metabolic syndrome serves a useful purpose in that it emphasizes risk factor clustering and the importance of insulin resistance. However, it does not include other factors known to be strongly correlated with CV risk. CMR encompasses those risk factors that predispose an individual for diabetes and CV disease. It includes those factors in the definition of metabolic syndrome, as well as age, tobacco use, and LDL-C.

**Reference(s):**


**20. The Association’s Standards of Care endorse the preferred use of which of the following as a treatment target when triglycerides levels are >200 mg/dL because of ease of calculation and does not rely on any statistical estimates?**

A. LDL-C levels  
B. HDL-C levels  
C. Non-HDL-C levels  
D. Triglyceride/VLDL cholesterol ratio  
E. LDL-C/HDL-C ratio

**Answer:** C

**Rationale:**

Unlike LDL-C, non-HDL-C represents the cholesterol content that is present in all the atherogenic lipoproteins. Non-HDL-C was added in ATP-III as a secondary treatment target in patients with elevated triglycerides (>200 mg/dL), with a treatment target being 30 mg/dL above the LDL-C treatment target. The addition of non-HDL-C as a treatment target reflects the recognition of this calculated value as a predictive factor in CV disease. The Association’s Standards of Care still endorses this parameter.

The more recent ACC/AHA Guidelines on the management of cholesterol, however, makes no recommendation either for or against specific non-HDL–C goals for the primary or secondary prevention of arteriosclerotic CV disease.
Reference(s):


21. What formula is used to calculate non-HDL-C?

A. LDL-C level minus HDL-C level
B. Triglyceride level minus LDL-C level
C. Total cholesterol level minus HDL-C level
D. Total cholesterol level minus LDL-C level
E. Triglyceride level divided by 3 plus LDL-C level

Answer: C

Rationale:

Non-HDL-C is calculated as subtracting the HDL cholesterol level from the total cholesterol level (TC minus HDL cholesterol). It can also be calculated by dividing the triglyceride level by 5 and add that value to the LDL cholesterol level. The reference ranges for non-HDL-C are based on National Cholesterol Education III guidelines:

* Desirable: <130 mg/dL
* Borderline high: 139-159 mg/dL
* High: 160-189 mg/dL
* Very high: ≥190 mg/dL

Reference(s):


22. The more inclusive paradigm of CMR recognizes that:

A. Every risk factor should be weighted equally
B. The whole is not greater than the sum of its parts; that is, each risk factor has differential effects on future CV disease risk
C. Most markers have similar predictive importance for CV disease across all patients
D. None of the above
E. All of the above

Answer: B

Rationale:

CMR is continuous. That is, individuals have varying levels of CMR depending on the number and severity of their risk factors. When assessing a patient for comprehensive risk, a thorough documentation of the patient’s history should be done, including documentation of age, ethnicity, smoking status, physical activity level, diet, family history of premature CV disease risk or type 2 diabetes, and comorbidities. In addition, physical examination should include measurement of waist circumference and blood pressure (average of 3 readings), and calculation of body mass index. Lab results should include a fasting lipid panel, FPG, and creatinine or estimated glomerular filtration rate. A majority of these encompass CMR.

Evaluating patients for all contributory risk factors means there is more likelihood of identifying patients at high risk for CV disease or diabetes, allowing clinicians to intervene sooner with education and treatment. However, CMR recognizes that not all risk factors can be weighted equally, given their differential effects on future risk of CV disease or diabetes.

Reference(s):


23. Which of the following are major risk factors for developing type 2 diabetes?

A. Overweight/obesity
B. Increase in insulin sensitivity
C. Increased physical activity
D. Elevated HDL-C level
E. All of the above

Answer: A

Rationale:

Recognizing clinical signs and identifying risk factors in individuals at risk for developing diabetes are essential for preventing the onset of the disease. These signs/risk factors include insulin resistance, a lack of physical activity, and reduced HDL-C level. Having a BMI >25 kg/m² is defined as being overweight;
a BMI >30 kg/m² is defined as being obese. An elevated BMI is a risk factor for developing type 2 diabetes and should be assessed along with other risk factors to determine an individual’s level of CMR.

**Reference(s):**


**24. According to the Association’s Standards of Care, which of the following lipid parameters is a more accurate predictor of CV risk than serum total cholesterol levels, and thus is often the initial target for treatment?**

A. HDL-C  
B. LDL-C  
C. Triglycerides  
D. VLDL-C  
E. All of the above

**Answer: B**

**Rationale:**

Lipoprotein measurements are used to better assess CMR and prescribe tailored therapies to control blood lipids to reduce the risk of disease and related complications. Of these, LDL-C has traditionally been considered a more accurate predictor of CV risk than serum total-C level and is often the initial target for therapy, according to the Association’s Standards of Care. High levels of LDL-C can lead to and advance atherosclerosis.

However, the recent ACC/AHA Guidelines on Assessing CV risk employ a formula of various parameters, including gender, age, racial background (either Caucasian or African American, but not other ethnicities), SBP and blood pressure treatment, a ratio of total cholesterol to HDL-C, and the presence or absence of diabetes and tobacco use. The guideline committee did not employ LDL-C as a component of the risk calculator, nor does it make any recommendations either for or against specific LDL-C goals for the primary or secondary prevention of atherosclerotic CV disease.

**Reference(s):**


Case 2 Continuation

25. You discuss with FD the risk of being overweight. What does research data reveal about survival in individuals with a BMI of 30-35 kg/m²?

A. Life expectancy is decreased by 1-2 years
B. Life expectancy is decreased by 2-4 years
C. Life expectancy is decreased by 8-10 years
D. Life expectancy is not changed compared to patients with BMI of 25 kg/m²
E. Hazard is equivalent to smoking

Answer: B

Rationale:
In a collaborative analyses of baseline BMI versus mortality from 57 prospective studies, results revealed that median survival is decreased by 0–1 year for people who would, by about age 60 years, reach a BMI of 25–27.5 kg/m², decreased by 1–2 years for those who would reach 27.5–30 kg/m², and decreased by 2–4 years for those who would become obese (30–35 kg/m²). There was less information available for those with a BMI >35 kg/m², although median survival appears to be decreased by approximately 8–10 years in those who would become morbidly obese, that is a BMI of 40–50 kg/m².

Reference(s):

26. How does a body mass index (BMI) increase of 5 kg/m² impact SBP and DBP?

A. SBP is increased but DBP is decreased
B. Neither SBP nor DBP are affected
C. SBP is decreased but DBP is increased
D. Both SBP and DBP are increased
E. SBP and DBP are increased in males but not in females

Answer: D

Rationale:
In collaborative analyses of baseline BMI versus mortality from 57 prospective studies, results revealed that BMI (15–50 kg/m²) was associated positively (and nearly linearly) with both SBP and DBP. Results showed that on average across all ages (15–89 years), every increase in BMI of 5 kg/m² was associated with at least 5 mm Hg increase in SBP and approximately a 4 mmHg increase in DBP in both males and females.

Reference(s):
27. At the start of FD’s appointment, you take his BP. He comments that you do it differently than others who have taken his BP. Which of the following is CORRECT according to guidelines for the measurement of BP?

A. Measured while the patient is standing  
B. Feet dangling from the exam table without supporting the arm  
C. Immediately upon entering the exam room  
D. Cuff size should be appropriate for the upper arm circumference  
E. Elevated values should be confirmed later in the day

Answer: D

**Rationale:**
Measurement of blood pressure in the office should be done by a trained individual and follow the guidelines established for persons who do not have diabetes. These guidelines include taking measurements while patient is in a seated position and taken after 5 min of rest, feet are on the floor, and the cuffed arm is being supported at heart level. The cuff size should be appropriate for the upper arm circumference. If any blood pressures are elevated, those values should be confirmed on a separate day.

**Reference(s):**
American Diabetes Association. Standards of Medical Care in Diabetes—2014 *Diabetes Care*.  
2014;37:S14-S80.

28. Which of the following statements is TRUE regarding the age-specific relevance of blood pressure to vascular mortality in the general population?

A. A higher risk for CV events and mortality begins at a SBP/DBP of >115/75 mmHg and doubles for every 20-mmHg SBP or 10-mmHg DBP increase.  
B. A lower risk for CV events and mortality begins at a SPB/DBP of >115/75 mmHg and declines for every 20-mmHg SBP or 10-mmHg DBP decrease.  
C. A lower risk for CV events and mortality begins at a SBP/DBP of >120/80 mmHg and doubles for every 20-mmHg SBP or 10-mmHg DBP increase.  
D. A higher risk for CV events and mortality begins at a SBP/DBP of >135/85 mmHg and triples for every 10-mmHg SBP or 5-mmHg DBP increase.  
E. There is no increase in the risk of CV events and mortality related to increases in blood pressure.

Answer: A

**Rationale:**
Although much of the focus on CV disease risk has been on frank hypertension, it is clear that risks for CV disease increase at higher BP levels, even within the so-called normal range. An epidemiologic pooling study of nearly 1 million men and women revealed that risk of mortality from CV disease increases in a continuous fashion at SBP levels starting as low as 115 mmHg and DBP as low as 75 mmHg.

Within each decade of age at death, the proportional difference in the risk of vascular death associated with a given absolute difference in usual blood pressure is about the same down to at least 115 mmHg.
usual SBP and 75 mm Hg usual DBP, below which there is little evidence. At ages 40-69 years, each difference of 20 mmHg usual SBP (or, approximately equivalently, 10 mmHg usual DBP is associated with more than a twofold difference in the stroke death rate, and with twofold differences in the death rates from ischemic heart disease and from other vascular causes.

Reference(s):

29. The ACCORD trial examined whether blood pressure lowering to SBP <120 mmHg provides greater CV protection than a SBP level of 130–140 mmHg in patients with type 2 diabetes at high risk for CV disease. Which of the following prespecified endpoint(s) was significantly reduced by intensive blood pressure treatment?

A. All-cause mortality
B. Stroke and non-fatal stroke
C. CV mortality
D. Non-fatal myocardial infarction
E. All of the above

Answer: B

Rationale:
In ACCORD, blood pressure (BP) achieved in the intensive group was 119/64 mmHg and in the standard group 133/70 mmHg; the goals were attained with an average of 3.4 hypertensive medications per participant in the intensive group and 2.1 in the standard therapy group. The hazard ratio for the primary end point (nonfatal MI, nonfatal stroke, and CV death) in the intensive group was 0.88 (p = .20). Of the prespecified secondary end points, only stroke (p = .01) and nonfatal stroke (p = .03) were statistically significantly reduced by intensive BP treatment.

Reference(s):

30. With lifestyle modification, diet is a key component of managing a hypertensive patient with several CMR factors. Which diet would you recommend for FD to adopt to reduce his blood pressure?

A. A DASH eating plan
B. A Mediterranean diet eating plan
C. A variation of DASH with 10% protein replacement
D. Any of the above
E. None of the above

Answer: D

Rationale:
Non-pharmacological therapy is reasonable in individuals with diabetes who have mildly elevated blood pressure (SBP >120 mmHg or DBP >80 mmHg). If the blood pressure is confirmed to be ≥140 mmHg SBP and/or ≥80 mmHg DBP, pharmacological therapy should be initiated along with non-pharmacological therapy.

The most common food in Mediterranean-style diets are a higher intake of in fruits (particularly fresh), vegetables (emphasizing root and green varieties), whole grains (cereals, breads, rice, or pasta), and fatty fish (rich in omega–3 fatty acids); lower in red meat (and emphasizing lean meats); substituted lower-fat or fat-free dairy products for higher-fat dairy foods; and used oils (olive or canola), nuts (walnuts, almonds, or hazelnuts) or margarines blended with rapeseed or flaxseed oils in lieu of butter and other fats. When compared to individuals given minimal advice on dietary patterns, middle-aged or older adults with type 2 diabetes or at least 3 CVD risk factors who were counseled on a Mediterranean low-fat dietary pattern reduced BP by 6–7/2–3 mmHg. In an observational study of healthy younger adults, adherence to a Mediterranean pattern was associated with lower SBP/DBP (2–3/1–2 mmHg).

The DASH dietary pattern is high in vegetables, fruits, low-fat dairy products, whole grains, poultry, fish, and nuts, and rich in potassium, magnesium, and calcium, as well as protein and fiber. It is low in saturated fat, total fat, and cholesterol, sweets, SSBs, and red meats. In one study of adults with a SBP/DBP of 120–159/80–95 mmHg, whose body weight and sodium intake were kept stable, the DASH dietary pattern, when compared to a typical American diet of the 1990s, lowered SBP/DBP by 5–6/3 mmHg. The effect was seen in women and men, African American and non-African American adults, older and younger adults, and hypertensive and non-hypertensive adults.

In OmniHeart, variations of the DASH dietary pattern were compared to DASH. One dietary pattern replaced 10% of total daily energy with protein rather than carbohydrate; the other pattern replaced the same amount of carbohydrate with unsaturated fat. In adults with SBP/DBP of 120–159/80–95 mmHg, modifying the DASH dietary pattern by replacing 10% of calories from carbohydrates with the same amount of either protein or unsaturated fat (8% monounsaturated and 2% polyunsaturated) lowered SBP by 1 mmHg compared to the DASH dietary pattern. Among adults with SBP/DBP 140–159/90–95 mmHg, these replacements lowered SBP by 3 mmHg relative to DASH.

The Association’s Standards of Care recommend lifestyle therapy for elevated blood pressure, which consists of weight loss (if overweight); a DASH-style dietary pattern including reducing sodium and increasing potassium intake; moderation of alcohol intake; and increased physical activity.

Reference(s):


31. Which of the following statements is CORRECT regarding the daily requirement of sodium for individuals with hypertension?

A. Consume up to 4,000 mg of sodium per day.
B. Reduce sodium intake to below 1,500 mg per day.
C. Consume no more than 2,400 mg of sodium per day.
D. There is no maximum daily amount of sodium.
E. None of the above.

Answer: B

Rationale:
Reduction of sodium intake can lower BP an additional 2-8 mmHg. The most recent ACC/AHA guidelines recommend individuals with hypertension reduce their intake of sodium by at least 1,000 mg per day since that will lower BP, even if the desired level of sodium intake is not achieved, which is no more than 2,400 mg of sodium/day. If needed, further reduction of sodium intake to 1,500 mg per day is desirable, since it is associated with even greater reduction in BP. The Association’s Standards of Care recommend individuals with diabetes and hypertension reduce their sodium intake to below 1,500 mg/day.

Reference(s):

32. FD is taking amlodipine, a non-dihydropyridine calcium channel blocker (CCB) for BP control. For patients with CMR and elevated blood pressure, which class of drugs is recommended as the first choice treatment?

A. ACE inhibitor or ARB
B. Alpha blocker
C. Beta blocker
D. Non-dihydropyridine CCB
E. Diuretic

Answer: A

Rationale:
Lowering of BP with regimens based on a variety of antihypertensive drugs, including ACE inhibitors, ARBs, β-blockers, diuretics, and calcium channel blockers, has been shown to be effective in reducing CV events. The Association’s Standards of Care recommend pharmacological therapy for patients with diabetes and hypertension should be with a regimen that includes either an ACE inhibitor or an ARB. If one class is not tolerated, the other should be substituted. This conclusion is substantiated by results from a recent meta-analysis that showed ACE inhibitors may produce better outcomes in patients with diabetes...
than other antihypertensive medications. A meta-analysis of 63 randomized clinical trials reporting all-cause mortality, dialysis requirement and serum creatinine levels in persons with diabetes who received antihypertensive therapies evaluated treatments included ACE inhibitors, ARBs, alpha- and beta-blockers, calcium-channel blockers and diuretics, alone or in combination. Results indicated ACE inhibitors significantly decreased doubling of creatinine compared with placebo by 42%, whereas beta-blockers significantly increased mortality risk.

Reference(s):


Go AS, Bauman M, Coleman King et al. An effective approach to high blood pressure control: a science advisory from the American Heart Association, the American College of Cardiology, and the Centers for Disease Control and Prevention. Hypertension. 2013 Nov 15. [Epub ahead of print]

33. If BP is not controlled on monotherapy, combination antihypertensive therapy is recommended. In the action plan of your progress notes, which combination would you recommend if FD’s BP is not controlled in the future?

A. ACE inhibitor or ARB plus dihydropyridine CCB
B. Switch to an ACE inhibitor or ARB plus thiazide diuretic
C. ARB plus thiazide diuretic
D. Beta blocker plus thiazide diuretic
E. Alpha blocker plus dihydropyridine CCB

Answer: B

Rationale:
The American Society of Hypertension/International Society of Hypertension and National Institute for Health and Clinical Excellence guidelines recommend a RAAS inhibitor (ACE inhibitor or ARB) plus a CCB, whereas the ACC/AHA guidelines on the science advisory from the ACC/AHA/CDC underline the pivotal role of thiazide diuretics. The combination of a RAAS inhibitor with a CCB demonstrated the best efficacy in reducing CV endpoint. In ACCOMPLISH, the combination of an ACE inhibitor and CCB was shown to be beneficial in reducing the primary composite endpoint of CV events plus death from CV causes versus an ACE inhibitor plus thiazide diuretic. However, a subgroup analysis revealed the combination of an ACE inhibitor with a diuretic was more beneficial for those of African American origin or individuals with systolic heart failure.
Reference(s):


Case 2 Continuation

34. Part of your discussion with FD involves smoking cessation and its impact on his long-term treatment goals. With smoking cessation, what percent reduction in mortality could be expected for an individual with CHD?

A. 10%
B. 23%
C. 36%
D. 41%
E. 63%

Answer: C

Rationale:
The results of the INTERHEART study showed smoking even one cigarette per day can increase the risk of myocardial infarction (MI) by 5%. And results from a meta-analysis of the medical literature by Critchley et al revealed a 36% reduction in crude relative risk (RR) of mortality for patients with coronary heart disease (CHD) who quit compared with those who continued smoking. Thus, smoking cessation is associated with a substantial reduction in risk of all-cause mortality among patients with CHD.

Reference(s):

35. You want to test FD for type 2 diabetes. His FPG is 115 mg/dL. Each of the following would help to differentiate whether or not FD has diabetes EXCEPT:

A. A1c ≥6.5% performed in a laboratory using a method that is NGSP certified and standardized to the DCCT assay.
B. FPG (defined as no caloric intake for at least 8 hours) ≥126 mg/dL (7.0 mmol/L).
C. A 2-hour plasma glucose level during a 75-gram OGTT of 140 mg/dL (7.8 mmol/L) to 199 mg/dL (11.0 mmol/L).
D. A 2-hour plasma glucose ≥200 mg/dL (11.1 mmol/L) during a 75-gram OGTT.
E. In a patient with classic symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose ≥200 mg/dL (11.1 mmol/L).

Answer: C

Rationale:
This patient has an elevated FPG value between 100 and 125 mg/dL, also known as IFG, and the presence of IFG is highly predictive of type 2 diabetes and should be confirmed by an OGTT. If the OGTT 2-hour plasma glucose value is between 140 and 199 mg/dL, then the patient has IGT and prediabetes encompasses both IFG and IGT. A plasma glucose value of ≥200 mg/dL after an OGTT confirms a diagnosis of type 2 diabetes. An A1c measurement of >6.5% confirms the diagnosis of type 2 diabetes.

According to the Association’s Standards of Care, criteria for diagnosing diabetes are:

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>A1c &gt;6.5%.</td>
<td>The test should be performed in a laboratory using a method that is NGSP certified and standardized to the DCCT assay.*</td>
</tr>
</tbody>
</table>

OR

| FPG >126 mg/dL (7.0 mmol/L) | Fasting is defined as no caloric intake for at least 8 hours.* |

OR

| 2-h plasma glucose >200mg/dL (11.1mmol/L) during an OGTT | The test should be performed as described by the WHO, using a glucose load containing the equivalent of 75 g anhydrous glucose dissolved in water.* |

OR

| A random plasma glucose >200 mg/dL (11.1 mmol/L) | For persons with classic symptoms of hyperglycemia or hyperglycemic crisis |

* In the absence of unequivocal hyperglycemia, result should be confirmed by repeat testing

Reference(s):
Case 2 Continuation

FD’s lab results come back and his FPG is 118 mg/dL and A1c is 6.2%. You assess that he does not have type 2 diabetes and ask him to return in 6 months so you can reassess his adherence to your recommendations of lifestyle modifications and management of his hypertension.
**Case Study #3**

MR, a 37-year-old Hispanic male, comes in for an employment physical. He is currently employed as a garage mechanic, but is applying for a position as manager of a parts department in an automobile dealership. He states he has been overweight since childhood, as were his parents, but cannot lose weight, although he has tried many times. When trying to lose weight, he employed fad diets, some of which were successful. Once he lost as much as 20 pounds, but eventually regained the weight and rebounded past his baseline. MR does not exercise and leads a fairly sedentary life both at home and at work.

His family has recently begun to express concern about his risk of developing type 2 diabetes, and they have convinced him to seek medical consultation. The patient states he has not seen a physician in 2 years because he has not adhered to either his hypertension or cholesterol-lowering therapy.

Past medical history: hypertension and hypercholesterolemia; no surgeries.

Family history: both mother and father are alive and both are diagnosed with hypertension and type 2 diabetes.

Physical Examination: height, 5'11" (180.3 cm); weight, 362 pounds (164.5 kg); body mass index (BMI), 46.2 kg/m$^2$; waist circumference, 47 inches (119.3 cm); BP, 152/104 mmHg; heart rate, 82 bpm.

Laboratory results: total cholesterol 273 mg/dL; LDL-C 181 mg/dL; HDL-C, 37 mg/dL; triglycerides, 300 mg/dL; FPG, 113 mg/dL.

Social history: does not exercise; denies tobacco, illicit drug use; he drinks one or two beers a day after work with his friends.

Medications: telmisartan 80 mg once daily; simvastatin 20 mg once daily (prescribed but non-adherent with both).

Assessment: MR is a morbidly obese male, alert and oriented, in no acute distress. He is non-adherent to antihypertensive and lipid-lowering therapies.

**Questions 36-47**

36. What is the most poorly controlled risk factor for individuals with type 2 diabetes?

A. A1c  
B. Postprandial plasma glucose  
C. Body weight  
D. Waist circumference  
E. FPG

**Answer: C**

**Rationale:**

With a population-based mean BMI remaining in the obese range (33 kg/m$^2$) and waist circumference in the range defining abdominal obesity, excess body weight remains the most poorly controlled risk factor in those with type 2 diabetes. Study results show only 11% patients have a BMI <25 kg/m$^2$ and 16% meet the recommended waist circumference levels of ≤40 inches in males and ≤35 inches in females.
This has implications for long-term control of A1c and therefore the development of diabetes-related complications, including CVD, CKD, retinopathy and neuropathy

**Reference(s):**


**37. When taking this patient’s history of weight gain and loss over time, questions that should be asked include:**

A. Family history of obesity  
B. Dietary habits  
C. Level of physical activity  
D. Details of previous weight loss attempts  
E. All of the above  

**Answer: E**

**Rationale:**

To determine a direction for management of a person’s obesity, clinicians need to assess weight and lifestyle histories to determine potential contributory factors as to why they are obese. This assessment includes asking questions about history of weight gain and loss over time, details of previous weight loss attempts, dietary habits, physical activity, family history of obesity, and other medical conditions or medications that may affect weight. The answer can provide useful information about the origins of or maintaining factors for overweight and obesity, including success and difficulties with previous weight loss or maintenance efforts, as well as assist the clinician in determining any adjustments to the patient’s medical regimen and weight management efforts.

**Reference(s):**


38. For obese individuals with type 2 diabetes, most common perceived barriers to exercise include:

A. Lack of time and physical discomfort
B. Easily measure results
C. Can vary the goals depending on their desired outcome
D. Self-evaluation of progress
E. Goals can be re-evaluated and adjusted periodically to maintain the desired therapeutic effect

Answer: A

Rationale:
The promotion of physical activity requires some understanding of the principles of behavior change and of habit development. Additionally, barriers to physical activity and correlates of success with long-term exercise should be considered. Five components of behavior change and self-regulation include: the setting of realistic and simple goals, self-monitoring of personal behaviors linked to goal attainment, feedback about progress toward goals, self-evaluation of progress, and corrective behavior leading to effective movement toward goals.

For obese individuals with type 2 diabetes, the most common perceived barriers to exercise were lack of time and physical discomfort, although these barriers varied with age, gender and marital status. Exercises that are most likely to be successful in the long term are moderate in intensity, relatively inexpensive, simple, and convenient and include a social component. Parameters for a successful exercise program include being patient-appropriate, considers co-morbidities, is measurable, in a form that allows the HCP to address barriers and patient adherence, will vary depending on the desired outcomes, and is reevaluated and adjusted periodically to maintain the desired therapeutic effect.

Reference(s):


39. MR was able to lose weight but was not able to maintain that weight loss. Factors that contribute to a person’s inability to retain maximal weight loss include:

A. Socioeconomic status
B. An unsupportive environment
C. Compensatory changes in circulating hormones that encourage weight regain after weight loss is achieved
D. A and B above
E. All of the above

Answer: E

Rationale:
Long-term maintenance of weight, following weight reduction, is possible; however, research suggests an intensive program with long-term support is required. As a result, many individuals will regain a portion of their initial weight loss. Factors contributing to the individual’s inability to retain maximal weight loss include socioeconomic status, an unsupportive environment, and physiological changes, such as compensatory changes in circulating hormones that encourage weight regain after weight loss is achieved.

Reference(s):


40. In the Look AHEAD study, weight loss strategies associated with lower BMI in overweight or obese individuals with type 2 diabetes included:
A. Weekly self-weighing
B. Skipping breakfast
C. Increased intake of fast foods
D. Increasing physical activity
E. A and D above

Answer: E

Rationale:
In the Look AHEAD study, weight loss strategies associated with lower BMI in overweight or obese individuals with type 2 diabetes included weekly self-weighing, regular consumption of breakfast, and reduced intake of fast foods. Other successful strategies included increasing physical activity, reducing portion sizes, using meal replacements (as appropriate), and encouraging individuals with diabetes to eat those foods with the greatest consensus for improving health.

Reference(s):
41. According to guidelines for the management of obesity, what is the initial goal recommended for weight reduction?

A. 1% to 3%
B. 3% to 5%
C. 5% to 10%
D. 12% to 15%
E. >15%

Answer: C

Rationale:
Although 3% to 5% of body weight may lead to clinically meaningful reductions, in some risk factors for CV disease, larger weight losses produce greater benefits. The latest ACC/AHA/TOS guidelines recommend a 5% to 10% reduction of baseline body weight within 6 months as an initial goal. The Association’s Standards of Care note at least a 7% of reduction in body weight is recommended.

Reference(s):

42. MR has a history of hypertension. Each of the following has been shown to be implicated in the pathophysiology of obesity-related hypertension EXCEPT:

A. Increase in adiponectin
B. Increases in leptin levels
C. Renin-angiotensin-aldosterone system
D. Obstructive sleep apnea
E. Impairment in salt excretion

Answer: A

Rationale:
Obesity predisposes the kidney to reabsorb sodium by neural (SNS), hormonal (aldosterone and insulin), and renovascular (angiotensin II) mechanisms. Leptin is produced in adipocytes and secreted into plasma, where the circulating concentration reflects the fat mass of the individual. A potent appetite suppressant, leptin, like insulin, stimulates the SNS. With regard to the RAAS, several mechanisms have been thought to underlie its activation in obesity, including SNS stimulation of renin release and angiotensinogen production in adipose tissue, especially intra-abdominal adipocytes.

Other factors that may be implicated in the pathophysiology of obesity-related hypertension include a decrease in adiponectin, and obstructive sleep apnea, which stimulates the SNS. One study showed a
significant negative correlation between plasma adiponectin concentration and mean, SBP, and DBP, which suggests a decrease adiponectin level contributes to the clinical course of essential hypertension. Obstructive sleep apnea, a well-recognized complication of obesity, is associated with increased SNS activity; this activity persists during daytime wakefulness. Obesity-related hypertension can also be caused by a decrease in natriuretic peptides, resulting in a consequent impairment in salt excretion.

**Reference(s):**


**43. Based upon his BMI category, MR is a candidate for which of the following interventions?**

A. Diet and exercise  
B. Diet, exercise, and behavioral counseling  
C. Diet, exercise, and behavioral counseling; then pharmacotherapy  
D. Diet, exercise, and behavioral counseling; then bariatric surgery  
E. Diet, exercise, and behavioral counseling; pharmacotherapy; then bariatric surgery

**Answer: E**

**Rationale:**

Among overweight and obese adults, analyses of continuous BMI show that the greater the BMI, the higher the risk of fatal CHD and combined fatal and nonfatal CHD in both men and women. With dietary intervention in overweight and obese adults, average weight loss is maximal at 6 months with smaller losses maintained for up to 2 years, while treatment and follow-up tapers. Weight loss achieved by dietary techniques aimed at reducing daily energy intake ranges from 4 to 12 kg at 6-month follow-up. Thereafter, slow weight regain is observed, with total weight loss at 1 year of 4 kg to 10 kg and at 2 years of 3 kg to 4 kg.

The principal components of an effective high-intensity, on-site comprehensive-lifestyle intervention includes prescription of a moderately-reduced calorie diet; a program of increased physical activity; and the use of behavioral strategies to facilitate adherence to diet and activity recommendations. All 3 components should be included in the intervention.

If patients are unable to lose enough weight to meet weight or targeted health outcome goals with their current treatment, consider offering or referring them for more intensive behavioral treatment than currently being attempted, an alternate diet including options for meal replacement, referral to a nutrition professional and the addition of obesity pharmacotherapy may be appropriate. The clinician should also assess the patient’s medication regimen for drugs that may contribute to weight gain and consider
adjustments if medically appropriate. If patients are unable to lose enough weight to meet weight or targeted health outcome goals with their current treatment, consider offering or referring for more intensive behavioral treatment than currently being attempted, and the patient may be referred for evaluation for bariatric surgery.

According to the most recent clinical practice guidelines, those eligible for a bariatric surgical procedure include individuals with a BMI $\geq 40$ kg/m$^2$ who have no coexisting medical problems and for which the procedure would not be associated with excessive risks. In addition, individuals with a BMI $>35$ kg/m$^2$ and 1 or more severe obesity-related co-morbidities, which include (but not inclusive of) type 2 diabetes, hypertension, hyperlipidemia, OSA, OHS, or considerably impaired quality of life, may also be offered a bariatric procedure.

Although those with BMI of 30–34.9 kg/m$^2$ and with diabetes or at CMR may also be offered a bariatric procedure, current evidence is limited by the number of subjects studied and lack of long-term data demonstrating a net benefit. According to these guidelines, there is insufficient evidence for recommending a bariatric surgical procedure independent of BMI criteria specifically for glycemic control alone, lipid lowering alone, or CV disease risk reduction alone.

The following table outlines when weight-loss surgery is recommended after lifestyle modification and pharmacotherapy.

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Body Mass Index (Kg/m$^2$)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>25-26.9</td>
</tr>
<tr>
<td>Diet, physical activity, behavioral therapy</td>
<td>Yes with comorbidities*</td>
</tr>
<tr>
<td>Pharmacotherapy</td>
<td>NO</td>
</tr>
<tr>
<td>Weight-loss surgery</td>
<td>NO</td>
</tr>
</tbody>
</table>

* Include but not limited to type 2 diabetes, hypertension, hyperlipidemia, OSA, OHS

According to the 2008 NIH guidelines, based upon his BMI, MR is a candidate for diet, exercise, and pharmacotherapy for the management of his abdominal obesity, and a candidate for bariatric surgery if these other interventions fail to accomplish his target weight goal.

Reference(s):


Mechanick JI, Youdim A, Jones DB, et al. Clinical practice guidelines for the perioperative nutritional, metabolic, and nonsurgical support of the bariatric surgery patient-2013 update: co-sponsored by


**Case 3 Continuation**

44. MR has implemented improved nutrition, physical activity, and behavior therapy. Which of the following diets has been shown to improve CV risk factors, such as lipids, triglycerides, and blood pressure in persons with diabetes?

A. Mediterranean  
B. Vegetarian  
C. Low fat  
D. DASH  
E. A and D above

**Answer: E**

**Rationale:**

Although mostly studied in the Mediterranean region, the Mediterranean-style eating pattern has been observed to improve lipids, blood pressure, and triglycerides in persons with diabetes, as well as lowering combined end points for CV disease events and stroke when supplemented with mixed nuts (including walnuts, almonds, and hazelnuts) or olive oil. And for those following an energy-restricted Mediterranean-style eating pattern, improvements in glycemic control were also achieved.

In a review of vegetarian and low-fat vegan studies in individuals with type 2 diabetes, diets ranging in duration from 12 to 74 weeks did not consistently improve CV risk factors or glycemic control except when energy intake was restricted and a loss of weight was measured.

There is limited evidence on the effects of the DASH eating plan on health outcomes specifically in individuals with diabetes. One small study in individuals with type 2 diabetes revealed the DASH eating plan, which included a sodium restriction of 2,300 mg/day, improved A1c, blood pressure, and other CV risk factors. Despite this limited evidence, however, one would expect benefits of the DASH eating plan in controlling blood pressure and lowering risk for CV disease that is seen for the general population would also be beneficial for persons with diabetes.

**Reference(s):**


**45.** From a nutritional perspective, intake of which of the following has a direct effect on postprandial glucose levels in people with diabetes and is the primary macronutrient of concern in glycemic management?

A. Fats  
B. Carbohydrates  
C. Protein  
D. A and B above  
E. All of the above  

**Answer:** B

**Rationale:**

The primary macronutrient of concern in the glycemic management is carbohydrate. A meta-analysis showed that at 6 months, low-carbohydrate diets were associated with greater improvements in triglyceride and HDL-C concentrations than low-fat diets; however, LDL cholesterol was significantly higher on the low-carbohydrate diets.

**Reference(s):**


**46.** Which of the following statements is CORRECT regarding the effectiveness of nutritional therapy?

A. As an effective component of an overall treatment plan, nutrition therapy is recommended only for individuals with type 2 diabetes.
B. Individuals who have diabetes should receive individualized medical nutritional therapy (MNT) as needed to achieve treatment goals, preferably provided by an RD familiar with the components of diabetes MNT.

C. For individuals using fixed daily insulin doses, consistent carbohydrate intake with respect to time and amount has no impact for improving glycemic control and/or reduce the risk for hypoglycemia.

D. Despite cost savings from diabetes nutrition therapy, evidence shows no improved outcomes such as reduction in A1c.

E. Individuals with diabetes should receive DSME according to national standards and DSMS only when the diagnosis of diabetes is made.

**Answer: B**

**Rationale:**

DSME and DSMS are critical elements of care for all individuals with either type 1 or type 2 diabetes, and are necessary to improve outcomes in a disease that is largely self-managed. According to the latest nutrition therapy recommendations, individuals who have diabetes should receive individualized MNT as needed to achieve treatment goals, preferably provided by a registered dietician familiar with the components of diabetes MNT. For those administering fixed daily doses of insulin, consistent carbohydrate intake with respect to time and amount can result in improved glycemic control and reduce the risk for hypoglycemia. Persons with diabetes should receive DSME according to national standards and DSMS when their diabetes is diagnosed and as needed thereafter. In addition, diabetes nutrition therapy can result in cost savings and improved outcomes such as reduction in A1c.

**Reference(s):**


47. After instituting lifestyle modifications, MR still has a BMI of 39 kg/m². Your treatment plan is to next initiate pharmacotherapy if he had not achieved his target weight. Which of the following drugs are NOT APPROVED for the long-term management of abdominal obesity?

A. Orlistat
B. Sibutramine
C. Lorcaserin
D. Phenteramine-topiarmate
E. C and D above

**Answer: B**

**Rationale:**

There are currently 3 FDA-approved drugs for the long-term management of abdominal obesity: orlistat, lorcaserin, and phenteramine-topiarmate. Each are indicated as an adjunct to a reduced-calorie diet and increased physical activity for chronic weight management in adult patients with an initial body mass index (BMI) of:
- 30 kg/m² or greater (obese), or
- 27 kg/m² or greater (overweight) in the presence of at least one weight related comorbid condition, such as hypertension, dyslipidemia, type 2 diabetes.

If after 12 weeks on a maximal dose of the medication the patient has not lost at least 5% of initial body weight, the provider should reassess the risk-to-benefit ratio of that medication for the patient, and consider discontinuation of that drug.

Orlistat, a pancreatic lipase inhibitor that targets intestinal lipases, prevents the hydrolysis of triglycerides and absorption of fatty acids and monoacylglycerols from the gut. In a multicenter 57-week study versus placebo, orlistat demonstrated an 8.9% decrease in body weight ($p < .05$), an 0.18% decrease in A1c ($p < .05$), and a significant decrease in FPG levels ($p < .05$).

Lorcaserin affects central serotonin subtype 2A receptors, resulting in decreased food intake and increased satiety. It has been studied in obese patients with type 2 diabetes, producing approximately an average weight loss of 5.5 kg over the course of 12 months.

The effect of phentermine on chronic weight management is likely mediated by release of catecholamines in the hypothalamus, resulting in reduced appetite and decreased food consumption, but other metabolic effects may also be involved; the exact mechanism of action is not known. The effects of topiramate may be due to its effects on both appetite suppression and satiety enhancement, induced by a combination of pharmacologic effects. The phentermine-controlled-release topiramate formulation has been shown to decrease weight by an average of 12.2 kg over 52–104 weeks of treatment in various clinical studies.

Because of its effects on intestinal lipases, orlistat also causes socially unacceptable side effects, which include oily spotting, increased flatus with discharge, and fecal urgency. Thus, fat-soluble vitamin levels must be carefully monitored. Lorcaserin has been reported to increase the risk of psychiatric, cognitive, and serotonergic adverse effects and phentermine–topiramate may increase the risk of metabolic acidosis, glaucoma, and psychiatric and cognitive adverse effects.

FDA approval of phentermine–topiramate required a REMS, which includes a medication guide, a patient brochure, and a formal training program for prescribers. This program informs both patients and prescribers of the teratogenic risk and stress the need for women of reproductive potential to use effective forms of contraception. REMS also permits only specially certified pharmacies to dispense phentermine–topiramate.

Sibutramine is a central inhibitor of norepinephrine and serotonin reuptake and, to a lesser extent, dopamine reuptake. Although shown to significantly decrease abdominal adiposity, lower triglyceride and raise serum HDL-C levels, it was removed from the market due to unacceptable side effects, specifically myocardial infarction and stroke.

Reference(s):


Case Study #4:

ERL, a 12-year-old Caucasian male, comes in for a school physical accompanied by his mother.

Physical exam: height, 5’5” (165 cm); weight, 195 lbs (88.6 kg); BMI, 32.5 kg/m²; waist circumference: 32” (81.3 cm); SBP: 132 mmHg; DBP: 80 mmHg (average of 3 readings); pulse: 84 beats per minute (average of 3 readings).

Family history: Both parents are alive, but overweight due to lack of physical activity; both employed full time as computer programmers; father has hypertension and diabetes; mother was told she has prediabetes. Neither parent exercises nor are involved in any structured activity program.

Social history: ERL denies tobacco use, alcohol intake, or illicit drug use; has no structured exercise program as his school discontinued gym classes; spends 3-4 hours a day playing video games; another couple of hours a day on the computer doing his homework. He enjoys snack foods, especially potato chips and drinking sugar sweetened beverages.

Lab results (within the past week): A1c, 6.4%; FPG, 105 mg/dL; total cholesterol, 240 mg/dL; LDL-C, 165 mg/dL; HDL-C, 31 mg/dL; triglycerides, 220 mg/dL.

Medications: None; all of his vaccinations are up-to-date.

You document ERL has several factors related to CMR and prescribe treatment with the goal of preventing him from progressing to type 2 diabetes.

Questions 48-58

48. According the Association’s Standards of Care, each of the following meet the parameters for CMR factors in this patient EXCEPT:

A. FPG ≥90 mg/dL.
B. Waist circumference >40 inches (102 cm) in males; >35 inches (88 cm) in females
C. BP ≥130/85 mmHg.
D. HDL-C level ≤40 mg/dL in males.
E. Triglyceride level ≥150 mg/dL.

Answer: A

Rationale:

A comprehensive risk assessment should include a thorough documentation of the patient’s history (age, ethnicity, smoking status, physical activity level, diet, family history of premature CV disease or type 2 diabetes, and comorbidities), physical examination (BMI, waist circumference, and BP), and laboratory test results (FPG, creatinine or estimated glomerular filtration rate, and fasting lipid profile). This assessment should help guide the clinician to determine the level of CMR in any given patient. However, this assessment should not be reserved strictly for adults, but starts at a much younger age.

According to the Association’s Standards of Care, parameters of CMR are highly concordant; in aggregate they enhance risk for coronary heart disease at any given LDL-C level. Parameters for factors in adults risk include:

- FPG ≥110 mg/dL.
• Waist circumference >40 inches (102 cm) in males; >35 inches (88 cm) in females
• Blood pressure ≥130/85 mmHg.
• HDL-C level ≤40 mg/dL in males; ≤50 mg/dL in females.
• Triglyceride level ≥150 mg/dL.

However, the diagnosis of CMR in children and adolescents requires the assessment of the waist circumference (or BMI), SBP/DBP, lipids, and plasma glucose levels. Parameters for children/adolescents were fixed for blood pressure, lipids and glucose; abdominal circumference points and assessed by percentile although, the cut-offs for metabolic and blood pressure variables were not well defined in children aged 6-10 years; therefore, only adiposity levels were evaluated (considering waist circumference above the 90th percentile). The same criteria would be used for children aged 10-16 as in adults: FPG ≥100 mg/dL, triglycerides ≥150 mg/dL, HDL-C <40 mg/dL or the use lipid lowering drugs were considered risk factors as well SBP ≥130 or DBP ≥85 mmHg.

In a study of individuals ranging in age from 2 to 39 years who died from various causes (principally trauma), antemortem data revealed the presence of CV risk factors, including increased BMI, SBP and DBP, and serum concentrations of total cholesterol, triglycerides, LDL-C, and HDL-C. As a group, these risk factors were significantly associated with the extent of lesion formation in the aorta and coronary arteries (p < .001). The mean percentage of the intimal surface covered by lesions in patients with different numbers of risk factors (0, 1, 2, and 3 or 4) was reported, although a percentage increase for each individual risk factor was not. For individuals with 0, 1, 2, and 3 or 4 risk factors, the percentage of intimal surface covered with fatty streaks in the aorta was 19.1%, 30%, 38%, and 35%, respectively (p for trend = .01). In the coronary arteries, 1.3%, 2.5%, 8%, and 11%, respectively (p for trend = .01) was involved with fatty streaks and 0.6%, 0.7%, 2.4%, and 7.2%, respectively was involved with collagenous fibrous plaques (p for trend = .003). In the coronary arteries, the extent of fatty-streak lesions was 8.5x as great for individuals with three or four risk factors versus those with no risk factors (p = .03) and the extent of fibrous-plaque lesions in the coronary arteries was 12x as great (p = .006).

Reference(s):


49. What of the following statements is CORRECT regarding ramifications of children/adolescents being overweight or obese?

A. They are twice as likely to become overweight or obese adults as their non-obese peers.
B. They are 3 times as likely as to become overweight or obese adults as their non-obese peers.
C. They are 5 times as likely as to become overweight or obese adults as their non-obese peers.
D. They are 7 times as likely as to become overweight or obese adults as their non-obese peers.
E. There are no long-term risks for children who are overweight or obese.

Answer: C

Rationale:

Estimates from the NHANES indicate approximately one third of children in the U.S. are overweight or obese, with approximately 17% meeting criteria for obesity, as measured by a BMI score ≥95th percentile. Overweight or obese preschoolers are five times as likely as to become overweight or obese adults as their non-obese peers. In an analysis of the literature, all included studies consistently report an increased risk of overweight and obese youth becoming overweight adults, suggesting that the likelihood of persistence of overweight into adulthood is moderate for overweight and obese youth. Because of the effects of obesity on insulin resistance, weight loss is an important therapeutic objective for overweight or obese individuals who are at risk for diabetes. Therefore, preventing obesity early in life is a public health priority to improve health across the lifespan of an individual.

Reference(s):


50. Potential negative psychological outcomes in overweight children include all of the following EXCEPT:

A. High self-esteem
B. Depressive symptoms
C. Poor body image
D. Attention-deficit hyperactivity disorder
E. Sleep problems

Answer: A

Rationale:
A systematic review of the literature concluded the health consequences of childhood obesity have significant short-term and long-term adverse medical and psychosocial effects extending into adulthood. These include health-related physical outcomes, such as high blood pressure; high cholesterol; metabolic syndrome; type 2 diabetes; orthopedic problems; sleep apnea; asthma; and fatty liver disease, as well as psychological, social, and behavioral consequences, such as risk for problems related to body image; self-esteem; social isolation and discrimination; depression; and reduced quality of life.

Reference(s):

Case 4 Continuation
51. You recommend to ERL’s mother that she focus on lifestyle modifications for her son. Lifestyle modifications for managing CMR include:

A. Healthful diet
B. Weight loss
C. Calorie restriction
D. Increased physical activity
E. All of above

Answer: E

Rationale:
The primary treatment of elevated CMR is lifestyle modification. This includes regular exercise (3 to 5 days per week; 30 to 60 minutes per day), coupled with improved diet/nutrition, and weight reduction through caloric restriction of at least reduction of 500 kcal per day, regardless of diet composition. The goal is to achieve a sustainable weight loss of no more than 0.5 kg per week for those who are overweight.

Reference(s):

52. Strategies to reduce energy intake in children and adolescents include increasing which of the following?

A. Consumption of high energy-density foods
B. Consumption of fruits and vegetables
C. Consumption of sugar-sweetened beverages
D. Time spent watching television and exposure to food marketed to children.
E. All of the above

Answer: B
**Rationale:**

Environmental determinants of childhood obesity in the United States include shifts in food consumption, decreases in physical activity levels, and higher levels of television viewing, with the consequent inactivity and marketing of food to children. Intervention programs should focus on strategies that alter the food and physical activity environments in places where children live, learn, work, and play. These strategies include decreasing consumption of high energy-density foods, decreasing consumption of sugar-sweetened beverages (SSBs) and red meats, and decreasing time spent watching television and exposure to food marketed to children.

Large increases in the consumption of SSBs have coincided with the epidemics of obesity and type 2 diabetes. Results of a meta-analysis of 8 prospective cohort studies revealed a diet high in consumption of SSBs was associated with the development of type 2 diabetes. And those individuals in the highest (versus lowest) quintile of SSB intake had a 26% greater risk of developing diabetes.

To positively impact reduction in LDL-C, ERL’s mother can plan meals that emphasize the intake of vegetables, fruits, and whole grains, as well as low-fat dairy products, poultry, fish, legumes, non-tropical vegetable oils and nuts. This type of dietary pattern can be adapted to appropriate calorie requirements, personal and cultural food preferences, and nutrition therapy for other medical conditions, including individuals with diabetes. In addition, ERL should reduce the percent of daily calories obtained from saturated (<7% of total calories) and trans fats.

**Reference(s):**


53. ERL plays video games for 3-4 hours a day. According to the American Academy of Pediatrics, what is the recommended timeframe for children to have entertainment-based screen time per day?

A. <1 hour  
B. <2 hours  
C. <3 hours  
D. <4 hours  
E. <5 hours

**Answer:** B

**Rationale:**
An average 8-year-old spends eight hours a day using various forms of media, and teenagers often surpass 11 hours of media consumption daily. Research shows that children who spent >2 hours per day watching television or using a computer were at increased risk of high levels of psychological difficulties, and this risk increased if the children also failed to meet physical activity guidelines. Thus, the updated guidelines from the American Academy of Pediatrics, children should be limited to less than two hours of entertainment-based screen time per day and shouldn’t have TVs or Internet access in their bedrooms. This updated guideline includes all forms of “screen media” like smart phones, tablets, TV, video games, Twitter, Facebook. Clinicians are encouraged to take a media history and ask 2 media questions at every well-child visit: How much recreational screen time does your child or teenager consume daily? Is there a television set or Internet-connected device in the child's bedroom?

Reference(s):


54. Routine physical activity has important, protective health benefits, including:

A. Improved blood glucose and lipid levels.
B. No significant change in SBP or DBP.
C. Possible increases in inflammation.
D. Increasing visceral fat accumulation.
E. No change in body weight.

Answer: A

Rationale:
Routine physical activity has important, protective health benefits. People who lead sedentary lives are at heightened risk for developing diabetes and CV disease. In fact, roughly 35% of coronary heart disease deaths in the U.S. can be attributed to an inactive lifestyle. Recent recommendations regarding physical activity from various groups affirm the primary role of exercise in preventing chronic disease and in maintaining health throughout the one’s lifetime. In addition, a considerable body of evidence shows that consistent exercise can reduce CV disease risk by improving lipid levels, lowering blood pressure, reducing inflammation and decreasing visceral fat accumulation. Furthermore, exercise helps control body weight; contributes to healthy bones, muscles and joints; reduces falls and moderates fall-related injuries among older adults; relieves symptoms of anxiety and depression and is associated with fewer hospitalizations, physician visits and medications.

It has been suggested that in order to obtain beneficial health effects, mainly in order to reduce CV risk factors, school-age children should participate in daily moderate to intense physical activities, for 60 minutes or more, and reduce sedentary behavior to less than two hours a day.

Reference(s):


**Case 4 Continuation**

ERL returns 6 months later without any success with lifestyle modification. His mother made nutritious meals and snacks, but he refused to eat them, still eating strictly snack foods and drinking sugar sweetened beverages. And he did not want to stop playing his video games. Thus, ERL’s weight increased 4 pounds.

**55. Based upon the number of ERL’s CMR factors, you decide to test for type 2 diabetes, despite the patient’s lack of symptoms. Criteria for testing for type 2 diabetes in asymptomatic children (persons aged 18 years and younger) include being overweight and which of the following, EXCEPT:**

A. Caucasian race  
B. African American race  
C. Maternal history of diabetes or GDM during the child’s gestation  
D. Family history of type 2 diabetes in first- or second-degree relative  
E. Signs of insulin resistance or conditions associated with insulin resistance, such as acanthosis nigricans, hypertension, atherogenic dyslipidemia, polycystic ovary syndrome, or small-for-gestational age birth weight

**Answer:** A

**Rationale:**
With the increase of type 2 diabetes in children, this group should be tested based upon certain criteria. Criteria for testing for type 2 diabetes in asymptomatic children (persons aged 18 years and younger) include being overweight (e.g., weight >120% of ideal for height) plus any two of the following risk factors: family history of type 2 diabetes in first- or second-degree relative; race/ethnicity (Native American, African American, Latino, Asian American, Pacific Islander); signs of insulin resistance or conditions associated with insulin resistance (acanthosis nigricans, hypertension, dyslipidemia, polycystic ovary syndrome, or small-for-gestational-age birth weight); maternal history of diabetes or GDM during the child’s gestation. Testing should be initiated at 10 years of age or at onset of puberty, if puberty occurs at a younger age, and should be repeated every 3 years.

**Reference(s):**


56. Among children and adolescents, what percentage of new diabetes cases is type 2 diabetes?

A. 1%
B. 5%
C. 15%
D. 25%
E. 30%

**Answer:** C

**Rationale:**

In the 1980s, type 2 diabetes in teens was virtually unheard of. Unfortunately, over the last 30 years, the prevalence of childhood obesity has increased dramatically in North America. This prevalence has caused an increase in a variety of health problems, including type 2 diabetes, which previously was not typically seen until later in life. Although the prevalence of type 2 diabetes in teens is very low, it is estimated that 15% of new diabetes cases among children and adolescents are type 2 diabetes.

**Reference(s):**


**Case 4 Continuation**

Recent lab results reveal a FPG level of 134 mg/dL and an A1c of 7.3%. Assessment: ERL is diagnosed with type 2 diabetes. You continue to stress ERL find an activity that he would enjoy and that would “get him off the couch”. In addition, you recommend to his mother that she meet with a nutritionist to determine which nutritious foods he might eat. Now that ERL is diagnosed with type 2 diabetes, other interventions are needed.
57. Which of the following statements is INCORRECT regarding pharmacologic intervention(s) that are indicated to treat ERL’s type 2 diabetes and other parameters of his CMR?

A. TZDs are indicated for pediatric patients to treat hyperglycemia
B. Statins should NOT be started in an adolescent who has an LDL-C level >160 mg/dL
C. Aspirin (low dose) is NOT recommended in children or adolescents to reduce CV risk
D. Metformin and insulin are indicated for pediatric patients to treat hyperglycemia
E. All of the above

Answer: A

Rationale:

For children/adolescents with CMR factors, the initial treatment in this age-group is lifestyle modification; however, pharmacological treatments are indicated in the following cases: LDL-C is persistently over 190 mg/dL although risk factors are absent; presence of risk factors, such as obesity, hypertension or smoking and LDL-C over 160 mg/dL; and individuals with diabetes and an LDL-C over 130 mg/dL. Thus, to treat a lipid disorder, medications, such as statins, or other lipid-lowering therapies, including bile acid–binding resins (cholesteryramine), and cholesterol absorption inhibitors, each of which are currently available for treatment of dyslipidemia in children and adolescents.

Despite the escalating rates of obesity-driven type 2 diabetes in youth, oral pharmacologic interventions remain limited to metformin, the only FDA-approved oral hypoglycemic agent for children. If metformin fails to achieve target goals, insulin is the other choice. Thiazolidinediones do not have an FDA-approved indication for treating children/adolescents with type 2 diabetes.

For CV protection, low dose aspirin is recommended only for most men over the age of 50 and women over the age of 60 with diabetes who have one or more additional heart disease risk factors. For those with diabetes and a history of CV disease, aspirin (75-162 mg per day) is recommended in adults for secondary prevention; however, the use of aspirin in persons under the age of 21 is contraindicated due to the associated risk of Reye Syndrome.

Reference(s):


58. Which of the following statement is INCORRECT regarding the results of the TODAY Trial in adolescents with type 2 diabetes:

A. Dyslipidemia and chronic inflammation were common in youth with type 2 diabetes and improved over time.

B. Dyslipidemia and chronic inflammation were not commonly observed in youth with type 2 diabetes.

C. Those who failed to maintain glycemic control at the end of the trial had severe impairment of β-cell function at baseline and experienced progressive and faster loss of β-cell function compared with those with durable glycemic control.

D. Those who maintained glycemic control at the end of the trial had severe impairment of β-cell function and experienced progressive and faster loss of β-cell function compared with those with durable glycemic control.

E. A and D above

Answer: E

**Rationale:**

The TODAY Trial evaluated adolescents with type 2 diabetes, who were randomized to receive metformin, metformin plus rosiglitazone (a TZD), or metformin plus ILI. Participants (N=699) were tested periodically with an OGTT to determine insulin sensitivity, insulinogenic index or C-peptide index, and β-cell function relative to insulin sensitivity. Study results showed the combination of metformin plus rosiglitazone exhibited a significantly greater improvement in insulin sensitivity and β-cell function relative to insulin sensitivity during the first 6 months versus metformin monotherapy and versus metformin plus lifestyle. Although these improvements were sustained over 48 months of the trial, the participants who failed to maintain glycemic control had significantly lower β-cell function (~50%), higher fasting glucose concentration, and higher A1c at randomization compared with those who did not fail.

For those with a LDL-C >130 mg/dL or triglycerides ≥300 mg/dL, statin drugs were initiated. Various parameters of dyslipidemia and inflammation were measured over the course of 36 months or until loss of glycemic control, including lipids, apolipoprotein B (apoB), LDL particle size, hsCRP, homocysteine, PAI-1, and A1c. Results showed that dyslipidemia and chronic inflammation were common in adolescents with type 2 diabetes and worsened over time. Despite some treatment group differences in lipid and inflammatory marker changed over time, diabetes treatment was generally inadequate to control this worsening risk.

**Reference(s):**


**Case Study #5**

GRL, a 36-year old Caucasian male who is a staff sergeant in the Army, returns home from a 15-month deployment in Afghanistan. He was stationed in the mountains in the northeast section of the country on the Pakistani border. During his time there, his unit met resistance and were involved in intense “fire fights” every night. Along with the intensity of battle and being at an elevation of 10,000 feet, GRL had great difficulty in sleeping, which has continued upon his return to the U.S. He presents to you with clinical depression, caring about nothing, including his family or those around him.

Physical exam: height, 173 cm (5’ 8”); weight, 98 kg (216 lbs); BMI, 32.7 kg/m²; waist circumference, 34 inches; SBP, 125 mmHg; DBP, 82 mmHg (average of 3 readings).

Social history: 8-12 cans of beer daily; 2 pack-a-day smoker; maintains a state of physical fitness through daily calisthenics.

Family history: Both adopted mother and father are alive and well; he does not know the medical history of his birth parents.

Lab results: A1c, 6.1%; fasting blood glucose, 100 mg/dL; total cholesterol, 275 mg/dL; LDL-C, 160 mg/dL; HDL-C, 33 mg/dL; triglycerides, 210 mg/dL.

Medications: None

Assessment: a 35-year old male suffering from post-traumatic stress disorder, prediabetes, and dyslipidemia.

**Questions 59-65**

59. Which of the following statements is CORRECT regarding PTSD and CMR?

A. PTSD is simply a psychiatric disorder and not an important predictor for cardiac and metabolic disorders.

B. PTSD is an isolated disorder that is only seen in combat military veterans.

C. Military veterans diagnosed with PTSD are at higher risk of developing insulin resistance and metabolic syndrome than their counterparts without PTSD.

D. Individuals with PTSD have significantly less coronary artery disease and a lower mortality risk.

E. A and C above

Answer: C

**Rationale:**

PTSD is not simply a psychiatric disorder that affects combat military veterans, but is a severely disabling neuropsychiatric anxiety disorder that develops in civilians, police officers, and others as a result of experiencing horrifying trauma/stress. Someone may experience, witness, or be confronted with an event or events that involved actual or threatened death or serious injury, or a threat to the physical integrity of self or others. The person's response involved intense fear, helplessness, or horror. PTSD is not limited to adults; it can happen in children.

Normally one relates PTSD to combat exposure, but other traumatic experiences, such as motor vehicle, motor vehicle accidents, and hurricanes, life-threatening illnesses, such as myocardial infarction (MI), can
also cause PTSD. Results of a meta-analysis showed clinically significant prevalence (16%) of PTSD symptoms after acute coronary syndromes (ACS); two-thirds of patients continue to suffer from PTSD two years after an MI.

This traumatic stress increases the risk for inflammation-related somatic diseases and early mortality. CMR is reflected by the increased health risks associated with stress and PTSD. As a result, obesity, dyslipidemia, hypertension, diabetes mellitus, and CV disease are prevalent among individuals experiencing PTSD.

Reference(s):


60. The prevalence of CMR in military veterans who were involved in combat and suffered from PTSD is:

A.  18%
B.  32%
C.  43%
D.  52%
E.  None of the above

Answer: C

Rationale:

Overweight and obesity among male veterans with PTSD strikingly exceeds national findings. In a study of 1,710,032 Veteran men and 93,290 Veteran women, Das et al reported that 73.0% were at least overweight, 32.9% were classified as obese, and 3.3% were found to be morbidly obese. This finding illustrates the pervasiveness of overweight and obesity among military veterans. In addition, the prevalence of the CMR in those with PTSD was 43%. The rates of CMR were higher in veterans than those observed among adults in the general population as reported in the NHANES.
Reference(s):


**61. PTSD influences CMR by causing:**

A. Lower mean levels of triglycerides.
B. Lower SBP/DBP.
C. Elevated FPG levels.
D. Elevated levels of HDL-C.
E. All of the above

**Answer:** C

**Rationale:**
In persons with PTSD, there is chronic, high-level SNS arousal relative to controls, which is evidenced by elevated plasma and 24-hour urinary catecholamine levels. Those with PTSD exhibit CV sympathetic activation with significantly higher heart rates and SBP/DBP levels relative to controls, even during sleep, with lower respiratory sinus arrhythmia. Sympathetic arousal plays a key role in activation of the renin-angiotensin-aldosterone system and the pathogenesis of hypertension, and CV remodeling. When compared with data from NHANES, military veterans had higher SBP and DBP levels:

- SBP (130.8 mmHg versus 122.1 [women] and 123.1 mmHg [men])
- DBP (81.7 mmHg versus 71.2 mmHg [women] and 74.4 mmHg [men])

The magnitude of the sympathetic response to mental stress is associated with increasing insulin resistance. Thus, the incidence and prevalence of CMR in military personal is remarkably high, and even higher than in the general population. In veterans, the most common identified risk factors for CMS were decreased levels of HDL-C (34%), CAD (21%), and diabetes (19%). The severity of PTSD symptoms correlated with increasing various parameters of CMR. Similar to increases in BP, when compared with data from NHANES, military veterans also tended to have:

- Higher mean triglycerides (189.5 mg/dL versus 132.3 mg/dL in women; 164.0 mg/dL in men from NHANES).
- Higher FPG (106.4 mg/dL versus 98.8 mg/dL [women] and 103.4 mg/dL [men])
- Lower HDL (42.7 mg/dl versus 55.8 mg/dL [women] and 45.3 mg/dL [men]).

Reference(s):


62. Which of the following statements is CORRECT regarding the relationship between PTSD, CMR, and depression or psychiatric disorders?

A. There is no relationship between PTSD and CMR on the development of depression.
B. PTSD is associated with increased rates of affective disorders, anxiety disorders, and substance abuse.
C. Women who have PTSD are twice as likely to develop a major depression.
D. Men who have PTSD are three times as likely to develop depression.
E. CMR was present in 25% of war veterans with PTSD, and approximately half had co-morbid depression.

**Answer: B**

**Rationale:**

PTSD is associated with increased rates of affective disorders, anxiety disorders, and substance abuse. Results of the National Comorbidity Survey indicate that at least one additional psychiatric disorder is present in 88.3% of men and 79.0% of women who have a history of PTSD. In addition, 59% of men and 44% of women who have PTSD meet the criteria for three or more psychiatric diagnoses. Women who have PTSD are approximately 4 times as likely to develop a major depression and greater than 4 times as likely to develop mania as women who do not have PTSD. Men who have PTSD are approximately 7 times as likely to develop depression and more than 10 times as likely to develop mania as men who do not have PTSD.

In military personnel, a variety of factors predispose these individuals to increased risk of developing CMR. High levels of stress, depression, poor sleep quantity and quality as well as unhealthy lifestyle habits such as tobacco use and restricted physical exercise, have all been linked to increased CV disease. Despite growing evidence, there is a lack of awareness of the roles of these additional risk factors among physicians treating military patients. Increasing knowledge of the relationship between these conditions and CMR will enable physicians to initiate a multi-targeted approach to impact outcomes in a positive nature.

Psychological factors are independently associated with an increased risk of both diabetes and CV disease. These factors include depressive and anxiety symptoms, hostility, anger, and pessimism. Rates of CMR in patients with a psychiatric disorder is remarkably high, with 72% in patients with PTSD, 60% in those with schizophrenia, 58% in those with mood disorder, and 56% in those with dementia. This relationship can be partially correlated to PTSD and its effects on increasing those psychological factors.
The relationship between PTSD and CMR in military service personnel is multifaceted and the mechanisms seem to be associative rather than direct. However, a study identified CMS in 25% of war veterans with PTSD, and approximately half of these patients had co-morbid depression (47.8%).

Reference(s):


63. Individuals who use tobacco should be reminded that:
A. No matter how long they’ve smoked, their health will improve upon quitting.
B. Smoking aggravates cardiometabolic problems.
C. The risk of heart disease remains the same if they are long-time smokers.
D. Both a and b
E. All of the above

Answer: D

Rationale:
The deleterious effects of smoking are well known. About one in five deaths from CV diseases is attributable to smoking. And approximately 35,000 to 40,000 non-smokers die each year from CV disease as a result of exposure to environmental tobacco smoke. Research shows smoking aggravates cardiometabolic problems and doubles the risk for CV disease in patients with diabetes and increases the risk of neuropathy, nephropathy and possibly retinopathy in people with diabetes. The risk of heart disease is cut in half just one year after quitting. After 5 to 15 years without smoking, the patient’s CV risk is comparable to someone who never smoked.

Reference(s):


**Case 5 Continuation**

Based upon recommendations from the Association’s Standards of Care, you refer GRL to a mental health specialist. Although he does not have diabetes, he has CMR factors that could predispose him to develop type 2 diabetes. Indications for referral to a mental health specialist (familiar with diabetes management) may include gross disregard for the medical regimen (by self or others), depression, possibility of self-harm, debilitating anxiety (alone or with depression), indications of an eating disorder, or cognitive functioning that significantly impairs judgment.
Case Study #6

JH is a 54-year-old female who presents to you with complaints of a severe skeletomuscular shoulder pain secondary to surgical repair of an AC separation and broken collarbone.

Family history: Mother is alive and has type 2 diabetes; underwent CABG at age 56 and a PCI with stent placement at age 72. Father died at age 76 from an M.I.

Social history: Denies tobacco use, exercises only occasionally, and does not pay attention to her nutrition.

Physical exam: blood pressure, 135/77 mmHg; BMI, 27 kg/m²; height, 5’4” (162.5 cm); waist circumference, 36 inches (91.4 cm).

Laboratory results: total cholesterol level, 210 mg/dL; LDL-C, 156 mg/dL; HDL-C, 39 mg/dL; triglyceride, 145 mg/dL; FPG, 104 mg/dL; A1c, 6.2%.

Current medications: none

Assessment: female with skeletomuscular shoulder pain and newly diagnosed dyslipidemia and prediabetes; a family history of type 2 diabetes and coronary artery disease.

Questions 64-71

64. JH has lipid levels that have increased significantly since her last appointment 18 months ago. You discuss with her prescribing medication to manage her cholesterol levels. When evaluating this patient’s target goal in the management of cholesterol, which of the following is/are true?

A. LDL-C goals are different depending on category of risk (e.g., 0–1 risk factors, multiple risk factors, people with CHD or risk equivalent like diabetes)
B. Cholesterol should be checked every year for patients >20 years of age
C. Ordering a non-fasting lipid panel is preferred to gauge the patient’s total cholesterol, LDL-C, HDL-C and triglycerides
D. A normal triglyceride level is <100 mg/dL
E. All of the above

Answer: A

Rationale: JH has CMR based upon her physical exam and lab results. Patients with at CMR or type 2 diabetes have an increased prevalence of lipid abnormalities, contributing to their high risk of CV disease. Thus it is important to monitor lipids to minimize adverse outcomes. For patients >20 years of age, cholesterol should be checked every 5 years. Ordering a fasting lipid panel is preferred to gauge the patient’s total cholesterol, LDL-C, HDL-C and triglycerides, and monitor for risk factors, which include SBP/DBP >140/90 mmHg; HDL-C <40 mg/dL (in men); family history of myocardial infarction before age 55: in males, >45 years; in females, >55 years.

<table>
<thead>
<tr>
<th>Number of Risk Factors</th>
<th>Recommended LDL-C Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-1 risk factor</td>
<td>≤160 mg/dL</td>
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</tbody>
</table>
### Multiple (2+) risk factors

| People with overt CV disease | <100 mg/dL |

According to the ATP-III and the Association’s Standards of Care, aggressive lowering of LDL-C is recommended for patients with known risk of CV disease to achieve levels <100 mg/dL, or if very high risk, as low as 70 mg/dL; target HDL-C >40 mg/dl for men, >50 mg/dL for women; and triglycerides <150mg/dL. Conversely, the recent ACC/AHA guidelines on the management of cholesterol do not recommend titrating therapies to a specific LDL-C target level. Rather, they recommend monitoring overall patient risk score once prescribed lipid-lowering therapy, specifically a statin.

The ACC/AHA guidelines recommend for individuals with diabetes who are 40 to 75 years of age, a moderate-intensity statin (a drug that lowers LDL-C by 30% to 49%) should be used, whereas a high-intensity statin is a reasonable choice if the patient also has a 10-year risk of atherosclerotic CV disease >7.5%.

**Reference(s):**


**65. Based upon JH’s waist circumference and waist-to-height ratio, she has visceral obesity. Which of the following proinflammatory markers can be measured to determine level of CMR?**

A. Adiponectin
B. hs-CRP
C. IL-6
D. Plasminogen activator inhibitor-1
E. All of the above

**Answer: E**

**Rationale:**

Inflammation is a potential mechanism linking obesity and CMR. Excess abdominal fat is believed to increase blood levels of free fatty acids, which can inhibit the regulation of glucose by insulin. Visceral obesity is also characterized by a proinflammatory, prothrombotic state with elevated levels of CRP, cytokines and other proteins that may promote heart disease. CRP concentrations are elevated predominantly in obese individuals who are also insulin resistant.
An unfavorable inflammatory status has been shown to be negatively associated with metabolic health in obese (BMI >30 kg/m²) and overweight (BMI <30 kg/m²) individuals. Other molecules thought to play a role in development of insulin resistance and increased risk of CV disease include PAI-1 and fibrinogen. Research shows metabolically unhealthy obese and non-obese individuals present with higher concentrations of these various cytokines, including CRP, TNF-α, IL-6, and PAI-1, and lower levels of adiponectin compared to their metabolically healthy counterparts.

Reference(s):


**66. CRP is an emerging marker of inflammation and may provide useful information to assess the risk of CV disease. Which of the following statements is/are true?**

A. CRP is an independent predictor of inflammation, insulin resistance and future CV disease events in patients with and without established CV disease.

B. Patients with low CRP levels have 1.5 to 4 times the risk of myocardial infarction than those with high CRP levels.

C. Elevated CRP levels are not influenced by smoking, chronic inflammation, obesity and estrogen.

D. All of the above

E. None of the above

**Answer: A**

**Rationale:**

Studies have consistently found CRP to be an independent predictor of inflammation, insulin resistance and future CV disease events in patients with and without established CV disease. Individuals with elevated CRP levels (>2.0 mg/L) have 1.5 to 4 times the risk of myocardial infarction than those with low CRP levels. Some studies suggest that high CRP levels in the setting of low LDL-C impart the same level of CVD risk as high LDL-C levels in the setting of low CRP. CRP levels are more likely to be elevated in obese, insulin resistant patients.

The updated guidelines on atherosclerotic CV risk use CRP as a differentiator for assessing individuals with higher risk assessments to determine management strategies.
Reference(s):
Davidson MH. Emerging therapeutic strategies for the management of dyslipidemia in the patients with the metabolic syndrome. *Am J Cardiol.* 2004;93:3–11.

67. Which of the following statements is CORRECT regarding adiponectin?

A. Is important because of its anti-inflammatory, anti-diabetic and anti-atherogenic properties
B. Higher adiponectin levels are associated with insulin resistance.
C. Is not important in mediating CMR factors.
D. None of the above
E. All of the above

Answer: A

Rationale:
Adiponectin is the only known anti-inflammatory protein whose circulating levels are decreased before type 2 diabetes. Insulin resistance and obesity are both associated with lower plasma adiponectin concentrations. Results of one study showed insulin-resistant subjects had significantly lower adiponectin concentrations ($p < .001$), in both obese and non-obese subjects as compared with either obese or non-obese insulin-sensitive subjects.

Reference(s):

Case 6 Continuation

68. You order a CRP level; results come back as 3.4 mg/L (high). Which intervention(s) would you recommend for JH?

A. Aspirin
B. Statins
C. Increased physical activity
D. All of the above
E. None of the above

Answer: D
Rationale:

Despite ongoing uncertainty about the value of assessing markers of inflammation or hypercoagulation, interventions that target these abnormalities have been shown to reduce CMR. Aspirin therapy has a strong role in CV disease prevention, especially in men, older women, and people with multiple CV disease risk factors. Guidelines recommend increased physical activity because evidence shows consistent exercise can reduce risk of CV disease by improving lipid levels, lowering blood pressure, reducing inflammation and decreasing visceral fat accumulation, positively impacting inflammatory markers, such as CRP. And statins are recommended for individuals with diabetes aged 40 to 75 years with LDL–C levels between 70 to 189 mg/dL, with or without evidence of clinical atherosclerotic CV disease, which includes acute coronary syndromes, or a history of MI, stable or unstable angina, coronary or other arterial revascularization, stroke, TIA, or peripheral arterial disease presumed to be of atherosclerotic origin.

Reference(s):


69. JH has prediabetes and a family history of diabetes. Which of the following statements regarding aspirin is CORRECT for individuals at high risk for CV events?

A. Aspirin is beneficial for primary prevention of CV events in individuals with no previous history of vascular disease and a low risk of CV disease.

B. Aspirin is recommended only for women with prediabetes who are not at increased risk for gastrointestinal tract, intracranial, or other bleeding.
C. The use of aspirin in the primary prevention of vascular events should be considered on a case by case basis depending upon absolute risks of the patient (i.e., age, gender, family history of premature vascular disease).

D. The appropriate aspirin dose for primary prevention is 325 mg once daily.

E. Aspirin may reduce cerebrovascular events in persons with diabetes irrespective of CRP level.

**Answer: B**

**Rationale:**

Aspirin has been shown to be effective for secondary prevention of CV morbidity and mortality in high-risk patients. However, two randomized controlled trials investigated the beneficial effects of aspirin specifically in patients with diabetes failed to show a significant reduction in CV disease endpoints. These results raise further questions about the efficacy of aspirin for primary prevention in people with diabetes.

Based upon results from the Antithrombotic Trialists’ Collaboration study, aspirin significantly reduced coronary heart disease events in men but not in women; however, it had no effect on stroke in men but significantly reduced stroke in women. For secondary prevention, gender differences on the effects of aspirin have not been observed. The Association’s Standards of Care recommend the use of aspirin therapy (75–162 mg/day) as a secondary prevention strategy in those with diabetes who have a history of CV disease; however, aspirin not recommended for those at low CV disease risk, as the low benefit is likely to be outweighed by the risks of significant bleeding. The American Association of Clinical Endocrinologists’ guidelines recommend aspirin for all persons with prediabetes who are not at increased risk for gastrointestinal tract, intracranial, or other bleeding.

In a subanalysis of the Japanese Primary Prevention of Atherosclerosis with Aspirin for Diabetes (JPAD) study, results revealed for those not taking aspirin, the incidence of cerebrovascular events was higher in those individuals with diabetes who had an elevated CRP level (>0.1 mg/L) versus those with a low CRP level (<0.1 mg/L). However, for those taking aspirin, no significant difference was noted in the incidence of the cerebrovascular events between the high CRP group and the low CRP group. Thus, aspirin therapy may reduce cerebrovascular events in persons with diabetes who have an elevated CRP level.

Advanced glycation end products (AGE) and/or their receptors are significantly positively correlated with adiposity, inflammation, dyslipidemia, and insulin resistance in adults. In the Targeting Inflammation Using Salsalate for Type-2 Diabetes (TINSAL-T2D) study, salsalate, a non-acetylated salicylate, lowered plasma glucose levels in participants with type 2 diabetes and positively influence markers of inflammation, decreasing levels of AGE (e.g., CRP and TNF-α) and increasing levels of adiponectin.

**Reference(s):**


JH asks about the risk of bleeding with aspirin. Which of the following statements is correct regarding the risk of MAJOR bleeding (gastrointestinal or intracranial) from aspirin use, especially in persons with diabetes?

A. Major bleeding is observed only at doses greater than 325 mg per day.
B. There is no significant increase in major bleeding in individuals with diabetes who take aspirin.
C. Major bleeding is not an issue in patients at high risk of a CV event
D. Diabetes is associated with an increased risk of major bleeding episodes only in those taking aspirin.
E. None of the above

Answer: B

Rationale:
Therapy with low-dose aspirin is used for the treatment of CV disease. It is recommended as a secondary prevention measure for individuals with moderate to high risk of CV events, that is, for patients with multiple risk factors such as hypertension, dyslipidemia, obesity, diabetes, and family history of ischemic heart disease. However, any benefit may be outweighed by the risks of significant bleeding. But is this true for individuals with diabetes when compared to those without?

In a population-based cohort that compared individuals being treated with low-dose aspirin (<300 mg/day) versus matched controls without aspirin use, results showed aspirin use was associated with a
greater risk of major bleeding in most of the subgroups investigated; however, there was no significant increase in major bleeding in individuals with diabetes. For participants with diabetes, there was an associated increase risk of major bleeding episodes irrespective of aspirin use. Thus, those with diabetes had a high rate of bleeding that was not independently associated with aspirin use.

**Reference(s):**


**71. Matching Question.**

In discussing the management of her cholesterol levels, JH asks what are the different types of medications and how do they work. Match the class of drugs with the appropriate mechanism of action.

<table>
<thead>
<tr>
<th>Drug Class</th>
<th>Mechanism</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. Statins</td>
<td>___ Activates an enzyme that enhances the breakdown of triglyceride-rich lipoproteins while increasing HDL-C</td>
</tr>
<tr>
<td>B. Cholesterol absorption inhibitors</td>
<td>___ Reduces the liver’s ability to produce VLDL</td>
</tr>
<tr>
<td>C. Fibrates</td>
<td>___ Lowers LDL-C by reducing the amount of cholesterol absorbed in the intestines and increases LDL receptor activity.</td>
</tr>
<tr>
<td>D. Niacin</td>
<td>___ Binds to bile acids in the intestines and prevent their reabsorption, leading to increased hepatic LDL-C removal from the blood.</td>
</tr>
<tr>
<td>E. Resins</td>
<td>___ Increasing hepatic LDL-C removal from the blood.</td>
</tr>
</tbody>
</table>

**Answer:** C, D, B, E, A

**Rationale:**

Niacin reduces the liver’s ability to produce VLDL. At a dose of 1 to 2 g per day it has been shown to increase HDL-C levels by 15% to 30% and decrease triglycerides. However, evidence from clinical
outcome trials, which included concomitant statin therapy, failed to show any benefit with niacin. The AIM-HIGH trial, a secondary prevention trial in patients with low HDL-C and elevated triglycerides that added extended-release niacin to simvastatin (and ezetimibe as needed to achieve LDL-C goals), was stopped owing to the clinical futility for demonstrating event reduction, despite significant HDL-C increases and a significant event rate.

Fibrates activate an enzyme that enhances the breakdown of triglyceride-rich lipoproteins while increasing HDL-C. These drugs lower triglycerides while raising HDL-C approximately 10% to 20%, effects thought to occur via peroxisome proliferator-activated receptor alpha activation. However, in the lipid arm of ACCORD, adding fenofibrate to simvastatin did not improve the primary CV end point.

Cholesterol absorption inhibitors lower LDL-C by reducing the amount of cholesterol absorbed in the intestines and increase LDL receptor activity.

Resins bind to bile acids in the intestines and prevent their reabsorption, leading to increased hepatic LDL-C removal from the blood.

Statin therapy has proven risk reduction in both primary and secondary prevention of cardiovascular disease. Statin monotherapy has been shown to reduce LDL cholesterol and triglycerides by 18–55% and 7–30%, respectively, and increase HDL by 5–15%. Currently, statins remain the first-line therapy among individuals with low HDL-C levels and significant CV risk who warrant intervention.

Reference(s):


