Diabetes Prevention & Metabolic Syndrome

Ann Marie Blair, DNP, FNP, NP-C, BC-ADM, CDE
Piedmont Columbus Regional
Presenter Financial Relationships Disclosure

Ann M. Blair, DNP, FNP, NP-C, BC-ADM, CDE:

Speaker’s Bureau: Sanofi
Learning Objectives

• Discuss the relationship of metabolic syndrome and chronic disease
• Discuss laboratory findings associated with metabolic syndrome
• Discuss the criteria for screening for prediabetes and defining prediabetes
• Discuss the development and implementation of a management plan to proactively evaluate patients with prediabetes
• Discuss the clinical evidence used to support the management of individuals with prediabetes
Metabolic Syndrome

- Risk factors occurring together that increase the risk for cardiovascular disease, stroke, type 2 diabetes and cancer
- Central Obesity and insulin resistance-most importance underlying factors of the syndrome
- Referred to as:
  - Dysmetabolic syndrome
  - Hypertriglyceridemic waist
  - Obesity syndrome
  - Metabolic syndrome X
  - Syndrome X
  - Cardiometabolic syndrome
  - Deadly Quartet
  - Insulin resistance syndrome
Metabolic Syndrome

- Risk for heart disease, diabetes, and stroke increases with the number of metabolic risk factors
- Risk is linked to overweight and obesity and a lack of physical activity
- Insulin resistance increases risk
- Becoming more common due to a rise in obesity rates among adults
- In the future, may overtake smoking as the leading risk factor for heart disease
Metabolic Syndrome

Local Metabolic Abnormalities
- Adipose Tissue
- Liver
- Skeletal Muscle
- Pancreas
- CNS

Systemic Metabolic Abnormalities
- Metabolic Syndrome
- Visceral Obesity
- Insulin Resistance
- Glucose Intolerance
- Dyslipidemia
- Hypertension

Systemic Disease
- Human Disease
- Cardiovascular Disease
- Liver Disease
- Diabetes
- Cancer
- Other
Pathogenesis

Factor structure of the metabolic syndrome.

- Insulin Resistance
  - Fasting Insulin
  - Fasting Glucose
- Obesity
  - Body Mass Index
  - Waist/Hip Ratio
- Lipids
  - HDL Cholesterol
  - Triglycerides
- Blood Pressure
  - Systolic BP
  - Diastolic BP

Richard Kahn et al. Dia Care 2005;28:2289-2304

©2005 by American Diabetes Association
Metabolic Syndrome

• Multiple definitions
  • World Health Organization
  • European Group for the Study of Insulin Resistance
  • National Cholesterol Education Program ATP III
  • American Association of Clinical Endocrinologists
  • International Diabetes Federation
  • American Heart Association & National Heart, Lung and Blood Institute (NHLBI)
Metabolic Syndrome: NCEP ATP III

Defined by three or more of the following criteria:

- Abdominal obesity: WC ≥102 cm in men and ≥88 cm in women
- Hypertriglyceridemia: ≥150 mg/dl (1.695 mmol/l)
- Low HDL-C: <40 mg/dl in men and <50 mg/dl in women
- High blood pressure (BP): >130/85 mmHg
- High fasting glucose: >100 mg/dl

National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III)
Metabolic Syndrome: WHO

Glucose intolerance, impaired glucose tolerance (IGT) or diabetes mellitus (DM), and/or insulin resistance, together with two or more of the components listed below:

- Raised arterial pressure, i.e., ≥140/90 mm of Hg
- Raised plasma triglyceride (≥ 150 mg/dl) and/or low HDL-C (<35 mg/dl in men and <39 mg/dl in women)
- Central obesity, i.e., waist/hip ratio (WHR) >0.9 in men and >0.85 in women and/or body mass index (BMI) >30 kg/m²
- Microalbuminuria, i.e., urinary albumin excretion rate ≥ 20 μgm/minute or albumin/creatinine ratio ≥ 30 μgm/mg
Central Obesity/Intra-abdominal Adiposity (IAA)

- Potential to influence metabolism and cardiometabolic risk
  - Alterations in secretion of adipokines

- Adiponectin, a cardioprotective adipokine
  - Reduced in abdominally obese individuals

- IAA promotes increased secretion of metabolites and biologically active substances
  - Glycerol
  - Free fatty acids (FFA)
  - Inflammatory mediators [e.g., tumor necrosis factor alpha (TNFα), interleukin-6 (IL-6)]
  - Plasminogen activator inhibitor-1 (PAI-1)
  - C-reactive protein (CRP)
Central Obesity and Inflammatory Risk

- **Vascular dysfunction**
  - Endothelial dysfunction
  - Microalbuminuria

- **Pro-inflammatory state**
  - Elevated CRP
  - Elevated inflammatory cytokines (TNF-α, IL-6)
  - Decreased adiponectin levels

- **Pro-thrombotic state**
  - Increased anti-fibrinolytic factors (PAI-1)
  - Increased fibrinogen
Associating Risk

• Sedentary/Inactive lifestyle
• Consumption of high-calorie, low-fiber fast foods
• Populations
  • People who have a personal history of diabetes
  • People who have a sibling or parent with diabetes
  • Women when compared with men
  • Women who have a personal history of polycystic ovarian syndrome
  • Mexican Americans (highest rate), followed by whites and blacks
Associating Risk

• The risk for serious health concerns such as coronary artery disease, hypertension, dyslipidemia, albuminuria, and a range of other conditions increases with increased Body Mass Index (BMI)

• Obesity is most commonly assessed by the BMI
  • Individuals with a BMI between 25 and 29.9 are considered overweight
  • Individuals with a BMI of 30 and above are considered obese
Associating Risk
Body Mass Index vs Waist Circumference

• Body Mass Index
  • Incorporates height and weight
  • Does not incorporate body composition (difference between excess fat and muscle, fat distribution), fitness, age, race, or gender

• Waist Circumference
  • More highly correlated with metabolic risk factors
  • NCEP ATP III
    • Men > 40 inches
    • Women >35 inches
Age-adjusted Prevalence of Obesity and Diagnosed Diabetes Among US Adults

Obesity (BMI ≥30 kg/m²)

1994

2000

2015

Diabetes

1994

2000

2015

CDC’s Division of Diabetes Translation. United States Surveillance System available at http://www.cdc.gov/diabetes/data
Prevalence of Diabetes in the United States

National Diabetes Statistics Reports, 2017

- Estimates of Diabetes and its Burden in the United States
- Centers from Disease Control and Prevention

**Diabetes**
- 30.3 million (9.4%)
- 23.1 million diagnosed
- 7.2 million undiagnosed
- 23.8% have Diabetes—but do not know it!

**Prediabetes**
- 84.1 million (18+ years old)
- 33.9% of U.S. population
- 65+ years: 23.1 million
Prediabetes

- Epidemiologic evidence suggests that the **complications** of type 2 diabetes begin early in the progression from NGT to frank diabetes
- Prediabetes and diabetes are conditions in which **early detection** is appropriate, because
  - Duration of hyperglycemia is a predictor of **adverse outcomes**
  - There are effective interventions to **prevent disease progression** and to reduce complications

NGT, normal glucose tolerance ; T2D, type 2 diabetes
Feasibility of Preventing Type 2 Diabetes

• There is a long period of glucose intolerance that precedes the development of diabetes
• Screening tests can identify persons at high risk
• There are safe, potentially effective interventions that can address modifiable risk factors:
  • Obesity
  • Body fat distribution
  • Physical inactivity
  • High blood glucose

Prediabetes Risk Test

Untreated individuals with prediabetes are at increased risk for diabetes as well as for microvascular and macrovascular complications. Treatment goals are to prevent deterioration in glucose levels and modify other risk factors such as obesity, hypertension, and dyslipidemia. The same blood pressure and lipid goals are suggested for prediabetes and diabetes. Intensive lifestyle management is the cornerstone of all prevention efforts; pharmacotherapy targeted at glucose may be considered in high-risk patients.
Policy Paradigm Shifts are Needed to Stem the Global Tide of Type 2 Diabetes

- Integrating **primary and secondary prevention** along a clinical continuum
- **Early detection** of prediabetes and undiagnosed diabetes
- Implementing **cost-effective prevention** and control by integrating community and clinical expertise and resources within affordable service delivery systems
- Sharing and adopting **evidence-based policies** at the global level

T2D, type 2 diabetes
184 million people 
have 
and 

$327B 
The total cost of diagnosed diabetes in the US in 2017
Interventions to Reduce Risks Associated with Prediabetes

- **Therapeutic lifestyle** management is the cornerstone of all prevention efforts
- **No pharmacologic agents** are currently approved for the management of prediabetes
  - Pharmacotherapy targeted at glucose may be considered in high-risk patients after individual risk-benefit analysis

Staggering Health Burden of Diabetes in the US: The Diabetes Crisis in Contemporary Context of Another Health Crisis

IN THE US, Diabetes CONTRIBUTES TO ON AVERAGE¹:

- 1 stroke every 2 minutes
- 1 case of ischemic heart disease every 80 seconds
- 1 case of kidney failure every 10 minutes
- 1 lower limb amputation every 5 minutes

In the US, 1 PERSON DIES EVERY 6½ MINUTES FROM DIABETES AND ITS COMPLICATIONS²

That's more than 218 people a day

IN THE UNITED STATES, IN 2016, 1 PERSON DIES EVERY 52 MINUTES FROM OPIOID OVERDOSE³

That's more than 46 people a day

¹ Type 1 or Type 2 Diabetes
Therapeutic Advances Over the Past 20 Years

ADA Standards of Care 1989

- Insulin
- SFU
- Meglitinide
- Basal insulin
- α-Glucosidase inhibitor
- Metformin
- TZD
- DPP-4 inhibitor
- SGLT-2 Inhibitor
- GLP-1R agonist
- Bromocriptine

Despite the Advancement and Investment we are Not Achieving our Goals

- **Decline in** % of patients at HbA1c <7%
- **At best, only about 50% of patients are at goal**
- **Increase in** % of patients with very poor control
- Unacceptable level of *morbidity* and *mortality*
- Diabetes-related costs to society are tremendous

ALL THIS DESPITE MORE THAN 40 NEW T2D TREATMENT OPTIONS APPROVED SINCE 2005

Cardiovascular (CV) Risk Factor Targets and CV Disease Event Risk in Diabetes: We are not getting the job done

Percent at target levels for any one, two, or all three factors among the 2018 persons with diabetes:

<table>
<thead>
<tr>
<th></th>
<th>Any 1 of 3</th>
<th>Any 2 of 3</th>
<th>3 of 3</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>41.1%</td>
<td>26.5%</td>
<td>7.2%</td>
</tr>
</tbody>
</table>

Percent CVD risk reduction for being at target level among the 2018 persons with diabetes for each of the measures:

<table>
<thead>
<tr>
<th></th>
<th>Blood pressure</th>
<th>LDL-C</th>
<th>HBA1c</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>17%</td>
<td>33%</td>
<td>37%</td>
</tr>
</tbody>
</table>

Percent lower adjusted risk of CVD events with one, two, or three risk factors at target level:

<table>
<thead>
<tr>
<th></th>
<th>Any 1 of 3</th>
<th>Any 2 of 3</th>
<th>3 of 3</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>36%</td>
<td>52%</td>
<td>62%</td>
</tr>
</tbody>
</table>

Lifestyle Intervention in Prediabetes

- Persons with prediabetes should **reduce weight by 5% to 10%**, with long-term maintenance at this level
- A program of regular **moderate-intensity physical** activity for 30-60 minutes daily, at least 5 days a week, is recommended
- A diet that includes **caloric restriction**, **increased fiber** intake, and (in some cases) **carbohydrate intake limitations** is advised

Intensive Lifestyle Intervention Effectively Prevents Progression from IGT to Type 2 Diabetes

Diabetes Prevention Program (N=3234)

- Intensive lifestyle intervention* (n=1079): 4.8 per 100 person-years, 58% reduction from baseline
- Metformin 850mg BID (n=1073): 7.8 per 100 person-years, 31% incidence
- Placebo (n=1082): 11 per 100 person-years

IGT, impaired glucose tolerance; T2D, type 2 diabetes


*Goal: 7% reduction in baseline body weight through low-calorie, low-fat diet and ≥150 min/week moderate intensity exercise
Effectiveness of Lifestyle Intervention for Diabetes Prevention Wanes as Weight Increases

Diabetes Prevention Program (N=3234)

- **Placebo**: 14.3
- **Metformin**: 7.0
- **Lifestyle**: 7.3

*Goal: 7% reduction in baseline body weight through low-calorie, low-fat diet and ≥150 min/week moderate intensity exercise

Lifestyle Intervention More Effectively Prevents Diabetes as Populations Age

Diabetes Prevention Program (N=3234)


*Goal: 7% reduction in baseline body weight through low-calorie, low-fat diet and ≥150 min/week moderate intensity exercise*
<table>
<thead>
<tr>
<th>Intervention</th>
<th>Follow-up Period</th>
<th>Reduction in Risk of T2D (P value vs placebo)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antihyperglycemic agents</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Metformin&lt;sup&gt;1&lt;/sup&gt;</td>
<td>2.8 years</td>
<td>31% (P&lt;0.001)</td>
</tr>
<tr>
<td>Acarbose&lt;sup&gt;2&lt;/sup&gt;</td>
<td>3.3 years</td>
<td>25% (P=0.0015)</td>
</tr>
<tr>
<td>Pioglitazone&lt;sup&gt;3&lt;/sup&gt;</td>
<td>2.4 years</td>
<td>72% (P&lt;0.001)</td>
</tr>
<tr>
<td>Rosiglitazone&lt;sup&gt;4&lt;/sup&gt;</td>
<td>3.0 years</td>
<td>60% (P&lt;0.0001)</td>
</tr>
<tr>
<td>Weight loss interventions</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Orlistat&lt;sup&gt;5&lt;/sup&gt;</td>
<td>4 years</td>
<td>37% (P=0.0032)</td>
</tr>
<tr>
<td>Phentermine/topiramate&lt;sup&gt;6&lt;/sup&gt;</td>
<td>2 years</td>
<td>79% (P&lt;0.05)</td>
</tr>
<tr>
<td>Bariatric surgery&lt;sup&gt;7&lt;/sup&gt;</td>
<td>10 years</td>
<td>75% (P&lt;0.001)</td>
</tr>
</tbody>
</table>

T2D, type 2 diabetes

Calorie Restriction

**Lowers HbA1c** in proportion to weight lost

9kg loss lowers HbA1c by about 0.9%*

**Other Benefits**

- Potential *remission of DM*
  - 46% at 1 year in DIRECT food substitution diet
- Reduction of **ASCVD risk factors**
- Reduction in use of **glucose-lowering drugs**
- Proven **safety**

An **individualized MNT** should be offered to all patients

All overweight and obese patients with diabetes should be advised of the health benefits of weight loss and encouraged to engage in a program of intensive **lifestyle management**, which may include food substitution
Physical Activity

• **Lowers HbA1c** by about 0.6%
• More is better
• **Supervised exercise** more effective than unsupervised
• Exercise has other health benefits
  • Reduction of ASCVD risk factors
  • Reduction of fall risk
  • Reduction of weight
  • Increase bone density
Relationship of Walking to Mortality Among US Adults with Diabetes

- **DESIGN**: Prospective cohort study
- **SUBJECTS**: 2896 adults, 1990 and 1991 National Health Interview Survey
- **RESULTS**: 

<table>
<thead>
<tr>
<th>Mortality</th>
<th>Inactive</th>
<th>2 hours/wk</th>
<th>3-4 hours/wk</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Cause</td>
<td>Ref 1.0</td>
<td>↓39%</td>
<td>↓54%</td>
</tr>
<tr>
<td>CV</td>
<td>Ref 1.0</td>
<td>↓34%</td>
<td>↓53%</td>
</tr>
</tbody>
</table>

**CONCLUSIONS**: Walking was associated with lower mortality across a diverse spectrum of adults with diabetes. One death per year may be preventable for every 61 people who could be persuaded to walk at least 2 h/wk.
Guidelines are Tools

• As a medical community our goal is to **improve patient outcomes**
• Evidence-based guidelines should assist the PCP and the patient in **shared decision making**
• The essence of the ADA-EASD Consensus statement on Management of Hyperglycemia is a focus on **patient factors and preferences** and the ever increasing choice of therapies available for glucose control
• The goals of diabetes care are to prevent short-term and long-term complications and optimize **quality of life**

Complex guidance leaves the PCP and the patient with a lot of work!
Consensus Report
Diabetologia https://doi.org/10.1007/s00125-018-4729-5

Diabetes Care 2018;41:1-33 https://doi.org/10.2337/dci18-0033
PREDIABETES ALGORITHM

IFG (100–125) | IGT (140–199) | METABOLIC SYNDROME (NCEP 2001)

LIFESTYLE THERAPY
(Including Medically Assisted Weight Loss)

TREAT ASCVD RISK FACTORS

WEIGHT LOSS THERAPIES

ASCVD RISK FACTOR MODIFICATIONS ALGORITHM

DYSLIPIDEMIA ROUTE

HYPERTENSION ROUTE

NORMAL GLYCEMIA

PROCEED TO HYPERGLYCEMIA ALGORITHM

OVERT DIABETES

TREAT HYPERGLYCEMIA
FPG > 100 | 2-hour PG > 140

1 PRE-DM CRITERION

MULTIPLE PRE-DM CRITERIA

Intensify Weight Loss Therapies

Low-risk Medications

Metformin

Acarbose

Consider with Caution

TZD

GLP-1 RA

LEGEND

Orlistat, lorcaserin, phentermine/topiramate ER, naltrexone/bupropion, liraglutide 3 mg, or bariatric surgery as indicated for obesity treatment

If glycemia not normalized

COPYRIGHT © 2017 AACE MAY NOT BE REPRODUCED IN ANY FORM WITHOUT EXPRESS WRITTEN PERMISSION FROM AACE. DOI 10.4158/EP161682-CS
Summary

Lifestyle is the foundation*
• Highly effective in motivated, adherent patients

Medications
• Lots of choices
• We hope to make it easier to navigate them
• Safety, efficacy, cost and convenience

Metabolic surgery*
• Consider it as very effective salvage therapy

*The only choices that can lead to disease remission
Lifestyle Take Home Points

- Diet and Exercise are **the cornerstones** of successful diabetes management (on or off medication)
- People with diabetes and the providers **need skills** to implement sustainable lifestyle intervention
- **Provider silence on lifestyle in unacceptable**
- Patient support in the form of diabetes self management education is crucial (**early and often)**
- If at first you don’t succeed-try something else!
Points for Discussion

• Diabetes Prevention and Remission
  • Diet and Obesity Treatment: What are the barriers?

• Support for Sustainable Effective Behavior Change
  • Who should orchestrate and how can it be supported?

• Comprehensive CVD Risk Management
  • Who should orchestrate?

• Guideline Harmonization: Who are we serving?
References


Centers for Disease Control. Prediabetes Risk Assessment https://www.cdc.gov/prediabetes/takethetest/


References


References

Standards of Medical Care in Diabetes—2019. (2019, January). *Diabetes Care,* 42 (Suppl.1)
