

# 2015 Treatment Guidelines for Diabetes (5<sup>th</sup> edition)

## 1. GUIDELINE OVERVIEW

- 1) Revised from the 2011 and 2013 Treatment Guideline for Diabetes, this guideline's purpose is to provide a treatment and management guidelines for diabetes for healthcare practitioners or professionals who are committed to treating diabetes in primary, secondary, and tertiary medical institutions throughout the country, on the basis of scientific evidence and clear benefits.
- 2) The guideline covers type 1 diabetes, type 2 diabetes, and gestational diabetes mellitus.

## 2. REVISIONS

### 1) CHAPTER 1. INTRODUCTION

- Criteria for diabetes diagnosis and classification were integrated into "Diagnosis and Classification of Diabetes Mellitus."
- "Diagnostic Criteria of Metabolic Syndrome" was deleted.

### 2) CHAPTER 2. MANAGEMENT OF DIABETES MELLITUS

- A recommendation for reducing the glycemic control target for adults with type 1 diabetes to <7.0% was added.
- Monitoring and Assessment of Glycemic Control  
A recommendation was added to perform the A1C test at least twice a year and conduct continuous glucose monitoring as part of glycemic control when the blood glucose fluctuation is severe or hypoglycemia is frequent.
- Lifestyle Modification
  - ① A suggestion was added that while strict reduction of protein from the early stage is not recommended for patients with diabetic nephropathy [A], they should avoid having high-protein food (20% of total calories) [C].
  - ② Definitions of glycemic index and glycemic load index, description of sugar alcohols, and artificial sweeteners in carbohydrates intake were deleted.
- Treatment of Diabetes
  - ① A recommendation on an insulin therapy for type 1 diabetes was added.
  - ② A recommendation was added encouraging the preferential use of metformin as the initial pharmacological monotherapy agent for type 2 diabetes.
  - ③ A recommendation on an injection therapy for type 2 diabetes was revised to include insulin and GLP-1 analogues.

- ④ A recommendation on treatment algorithm for type 2 diabetes was added to preferentially consider the presence of domestic clinical data, frequently prescribed agents, and adverse effects (e.g., increase in body weight, hypoglycemia) for the arrangement of agents. The A1C target was set to < 6.5%. If lifestyle modification does not attain this goal, metformin should be preferentially considered for antihyperglycemic agents. Patients can begin with a dual therapy if their A1C is  $\geq 7.5\%$  at diagnosis. Insulin therapy can be initiated from the beginning if A1C value is  $\geq 9.0\%$  at diagnosis and severe symptoms of hyperglycemia are diagnosed. If the pharmacological therapy combined with lifestyle modification does not achieve the glycemic control target within 3 months, blood glucose should be actively controlled by proceeding to the next stage.
- ⑤ "A Section for Surgical Treatment of Type 2 Diabetes" was revised to include "Bariatric Surgery."
  - Immunization
- ① Recommendations for influenza vaccination and pneumococcus vaccination were simplified.
  - Management of Diabetes Mellitus
- ① Management of hypertension, dyslipidemia, antiplatelet agent, smoking cessation, and cancer screening test of patients with diabetes were transferred to CHAPTER 2. MANAGEMENT OF DIABETES MELLITUS.
- ② A recommendation on target pressure of people with diabetes was revised to a systolic blood pressure goal of < 140 mm Hg, and a diastolic blood pressure goal of < 85 mm Hg.
- ③ A recommendation was added to adopt statins as the first-line agent to treat hypercholesterolemia.
  - A recommendation on the dose of aspirin, an antiplatelet agent, was specified as 100 mg/day considering the domestic condition.
  - Management for Special Situations: a recommendation on managing diabetes on sick days and education regarding hypoglycemia during driving was added.

### **3) CHAPTER 3. DIABETIC COMPLICATIONS**

- Diabetic Nephropathy
  - ① Because proteinuria is a continuous variable, the terms microalbuminuria (30-299 mg/24 h) and macroalbuminuria (> 300 mg/24 h) were revised to modestly elevated (30-299 mg/24 h) and higher ( $\geq 300$  mg/24 h) levels of urinary albumin excretion, respectively.
  - ② An angiotensin-converting enzyme (ACE) inhibitor or an angiotensin receptor II blocker is not recommended for the primary prevention in patients with diabetes who have normal blood pressure and normal urinary albumin excretion.
  - ③ For patients with diabetic nephropathy, excessive restriction of dietary protein intake ( $\leq 0.8$  g/kg/day) is not recommended
- Diabetic Retinopathy
  - ① If there is no evidence of retinopathy on examination, re-take of the examination after every 2 years is recommended.

- ② A recommendation was added to conduct treatment for diabetic macular edema with antivascular endothelial growth factor.

#### 4) CHAPTER 4. SPECIAL CASES OF DIABETES

- Diabetes and management before/after surgery were integrated into a subtitle, Glycemic Control in Hospitalized Patients or Patients with Severe Diseases.
- A section on diabetes in children and adolescents was deleted.
- Glycemic Control in Hospitalized Patients or Patients with Severe Diseases: A recommendation was added that A1C be measured if hyperglycemia is shown during hospitalization in patients who are not diagnosed but are at risk of diabetes.
- A section on diabetes in the elderly was added.

### 3. GRADING OF SCIENTIFIC EVIDENCE

The treatment guideline committee suggested a classification system to grade evidence (or guidelines) of the draft recommendations into four levels.

Evidence	Definition
A.	<b>Clear evidence on the recommendations:</b> Clear evidence from well-conducted, generalizable multicenter- and randomized controlled trials (RCTs) that are adequately powered, or clear evidence from a meta-analysis
B.	<b>Supportive evidence on the recommendations:</b> Supportive evidence from well-conducted cohort studies, or supportive evidence from well-conducted case-control studies
C.	<b>Possible evidence on the recommendations:</b> Evidence from randomized clinical trials that are not reliable but were conducted by small-size institutions; evidence from observational studies; and evidence from case reports
E.	<b>Expert recommendations:</b> Opinions from experts in the Korean Diabetes Association when there is no supportive evidence from clinical trials

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### **CHAPTER 3. DIABETIC COMPLICATIONS**

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### **CHAPTER 4. SPECIAL CASES OF DIABETES**

1. Treatment of Acute Diabetic Complications
2. Glycemic Control in Hospitalized Patients or Patients with Severe Diseases
3. Diabetes and Pregnancy
4. Diabetes in the Elderly

## CHAPTER 1. INTRODUCTION

### 1. Diagnosis and Classification of Diabetes Mellitus

#### I. Criteria for Diagnosis

##### 1. Normal blood glucose level

1-1. Fasting plasma glucose (FPG) <100 mg/dL; Fasting after not eating for at least 8 hours before the test

1-2. Two-hour plasma glucose level after 75 g glucose loading < 140 mg/dL

##### 2. Diabetes

2-1. A1C  $\geq$  6.5%, or

2-2 FPG  $\geq$ 126 mg/dL, or

2-3. Two-hour plasma glucose level after 75 g glucose loading  $\geq$  200 mg/dL, or

2-4. Typical symptoms of diabetes (polydipsia, polyuria, weight loss) and random plasma glucose  $\geq$  200 mg/dL

##### 3. Individuals (or groups) at high risk for diabetes

3-1. Impaired fasting glucose (IFG): FPG of 100–125 mg/dL

3-2. Impaired glucose tolerance (IGT): OGTT 2-hour plasma glucose level of 140–199 mg/dL (OGTT refers to oral glucose tolerance test.)

3-3. A1C of 5.7–6.4%

For 2-1, 2, or 3, in the absence of unequivocal hyperglycemia, repeat the same test on a different day to confirm the diagnosis.

A1C must be measured by a standardized method.

#### II. Classification

##### 1. Type 1 diabetes

Type 1 diabetes results from deficiency of insulin caused by beta cell destruction in the pancreas.

1-1. Immune-mediated diabetes

1-2. Idiopathic type 1 diabetes

##### 2. Type 2 diabetes

Type 2 diabetes results from insulin resistance and usually relative insulin deficiency.

##### 3. Other type

Due to genetic abnormalities of pancreatic beta cell function or insulin action, pancreatic disease, or drugs

##### 4. Gestational diabetes mellitus (glucose intolerance developing during pregnancy or diabetes diagnosed in the second or third trimester of pregnancy)

## 2. Screening and Diagnosis of Type 2 Diabetes Mellitus in Adults

1. Screening for type 2 diabetes is performed by fasting plasma glucose (FPG), oral glucose tolerance test (OGTT), or A1C test. [B]
2. Annual screening is recommended in adults aged  $\geq 40$ , or adults aged  $\geq 30$  with risk factors. [E]
3. If the fasting glucose value or A1C value are within the range below, additional testing is recommended. [C]
  - 3-1. Step 1: Measure fasting plasma glucose and A1C annually, if fasting plasma glucose is 100–109 mg/dL or A1C is 5.7–6.0%.
  - 3-2. Step 2: Conduct oral glucose tolerance test if fasting plasma glucose is 110–125 mg/dL or A1C is 6.1%–6.4%.
4. Because women with gestational diabetes mellitus (GDM) are at a high risk of developing type 2 diabetes mellitus, it is recommended to perform the 75-g OGTT at 6 to 12 weeks after delivery. If the test results remain normal, consider repeating the test every 3 years. [E]

### 3. Screening and Diagnosis of Gestational Diabetes Mellitus

#### I. Screening Test

1. All mothers should be tested for overt diabetes at their first prenatal visit by fasting plasma glucose (FPG), random plasma glucose, or A1C. [A]
2. Gestational diabetes mellitus (GDM) can be diagnosed by either of two strategies.
  - 2-1. Conduct a 2-hour 75-g OGTT at 24 to 28 weeks of gestation in pregnant women not previously known to have diabetes or GDM (one-step approach). [B]
  - 2-2. When using "two-step approach," conduct a 1-hour 50-g glucose loading test at 24 to 28 weeks of gestation in pregnant women not previously known to have diabetes or GDM. If the plasma glucose level measured 1-hour after the load is  $\geq 140$  mg/dL (or  $\geq 130$  mg/dL for mothers at high risk), proceed to a 100-g OGTT. [E]

#### II. Criteria for Diagnosis

1. An individual is diagnosed with overt diabetes if at least one of the following is met at the first prenatal visit. [B]
  - 1-1. Fasting plasma glucose (FPG)  $\geq 126$  mg/dL
  - 1-2. Random plasma glucose (RPG)  $\geq 200$  mg/dL
  - 1-3. A1C  $\geq 6.5\%$
2. The GDM diagnosis is made when at least one of the following is met according to the result of a 2-hour 75-g OGTT performed at 24 to 28 weeks of gestation. [B]
  - 2-1. Fasting plasma glucose (FPG)  $\geq 92$  mg/dL
  - 2-2. 1-hour plasma glucose  $\geq 180$  mg/dL
  - 2-3. 2-hour plasma glucose  $\geq 153$  mg/dL
3. If a 100-g OGTT is performed on the basis of the two-step approach, the GDM diagnosis is made when at least two of the following are met. [E]
  - 3-1. Fasting plasma glucose (FPG)  $\geq 95$  mg/dL
  - 3-2. 1-hour plasma glucose  $\geq 180$  mg/dL
  - 3-3. 2-hour plasma glucose  $\geq 155$  mg/dL
  - 3-4. 3-hour plasma glucose  $\geq 140$  mg/dL



#### **4. Prevention of Type 2 Diabetes Mellitus**

1. For individuals at high risk for developing type 2 diabetes (impaired fasting glucose, impaired glucose tolerance, or A1C of 5.7–6.4%), improving lifestyle habits (i.e., diet, exercise, and weight loss) helps to delay or prevent the development of type 2 diabetes. [A]
2. High risk individuals for developing type 2 diabetes should be actively counseled to not only reduce their body weight but also change lifestyle habits. [A]
3. The obese high-risk individuals for developing type 2 diabetes should target a loss of 5–10% from their initial body weight, and perform moderate-intensity exercise at least 150 min/week. [A]
4. An at least annual screening test for diabetes diagnosis is recommended for the high-risk individuals. [E]
5. Particular attention should be paid to the early screening and diagnosis for high-risk group. The government or medical societies should do their best to promote diabetes prevention projects. [E]

## CHAPTER 2. MANAGEMENT OF DIABETES MELLITUS

### 1. Glycemic Targets for Adults

1. Glycemic control is essential to reduce the risks of microvascular complications or macrovascular complications. [A]
2. In patients with type 2 diabetes, it is recommended to set a glycemic control target of A1C < 6.5%. [B]
3. The A1C target can be lowered for patients with short duration of diabetes, no significant complications, and little risk of hypoglycemia. [E]
4. Less stringent A1C goal can be appropriate for patients with frequent severe hypoglycemia, limited life expectancy, advanced microvascular or macrovascular complications, or the elderly aged  $\geq 75$  years. [B]
5. For self-monitoring of blood glucose, a fasting or preprandial glucose level of 80–130 mg/dL and postprandial glucose level <180 mg/dL are recommended. [E]
6. In patients with type 1 diabetes, it is recommended to set a glycemic control target of A1C < 7.0%. [A]

## **2. Monitoring and Assessment of Glycemic Control**

### **I. A1C test**

1. Although a 3-month A1C test is recommended, the interval depends on the patient's condition. [E]  
Perform the A1C test at least twice a year in patients with good glycemic control. [E]
2. A1C testing can be performed more frequently if the blood glucose fluctuation is severe; medication is changed; or more stringent control is needed (e.g., pregnancy). [E]

### **II. Self-Monitoring of Blood Glucose (SMBG)**

1. Patient education should be provided before using the glucometer. It is recommended to check instructions for use and evaluate the accuracy of the device every year. [E]
2. SMBG should be recommended for patients with type 1 diabetes or type 2 diabetes on insulin therapy. [A]
3. SMBG can help to control blood glucose for patients using noninsulin therapies. [E]
4. SMBG can be performed in various ways, before/after meals, at bedtime or dawn, before/after exercise, or in hypoglycemic condition. The SMBG frequency and timing vary with the patient's condition. [E]

### **III. Continuous Glucose Monitoring (CGM)**

1. CGM is useful to control blood glucose for patients with type 1 diabetes on multiple-dose insulin or insulin pump therapy. [A]
2. CGM can be performed as part of glucose monitoring when blood glucose fluctuation is severe or hypoglycemia is frequent. [E]

### 3. Medical Nutrition Therapy

1. People with diabetes and those in the high-risk group for diabetes should receive individualized medical nutrition therapy by a clinical dietitian. [A] Because medical nutrition therapy is cost-effective and improves outcomes, repeated education is recommended. [B]
2. Overweight or obese diabetic patients should reduce the energy intake while maintaining healthy eating patterns. [A]
3. In general, approximately 50% to 60% of total calories from carbohydrate is recommended. The intake of carbohydrate, protein, and fat should be individualized according to the patient's eating patterns, preferences, and metabolic goals. [C]
4. Strict restriction of protein intake is not recommended in the early stage of diabetic nephropathy, but high protein intake (>20% of total calories) should be avoided. [C]
5. Fat intake should be individualized by considering the patient's metabolic problems (e.g., obesity, dyslipidemia). Saturated fat, cholesterol, and trans-fat intake should be advised to the same level of the general public. [C]
6. Limiting sodium intake to 2000 mg/day (5 g of salt) is recommended. [E]
7. Additional vitamin or mineral supplementation is not necessary for people with diabetes. However, it should be recommended in the case of deficiency or limited dietary intake. [B]
8. To prevent diabetes, dietary fiber intake, including various sources such as whole grains, should be 20-25 g/day (12 g/1,000 kcal/day). [B]
9. Because alcohol consumption may increase the risk of hypoglycemia in diabetic patients with pharmacological therapy, it should be restricted to 1 to 2 drinks per day for those who show good glycemic control. Alcohol is prohibited for diabetic patients with liver disease, dyslipidemia, or obesity. [E]

#### **4. Exercise Therapy**

1. Patients with diabetes should be advised to perform at least 150 min/week of moderate-intensity aerobic exercise (50–70% of maximum heart rate), or at least 90 min/week of vigorous-intensity aerobic exercise (70% or higher maximum heart rate) spread over at least 3 days/week with no more than 2 consecutive days without exercise. [A]
2. In the absence of contraindications, adults with type 2 diabetes should be encouraged to perform resistance training at least twice per week. [A]
3. Request exercise prescription to an exercise specialist before starting physical activities, if necessary. [E]
4. Patients can be instructed to measure blood glucose before/after exercise to check the change of glucose level, and instructed to reduce diabetic agents or add snacks to prevent hypoglycemia. [E]
5. Because the risk of retinal hemorrhage or retinal detachment is high in patients with severe diabetic retinopathy, vigorous-intensity aerobic exercise or resistance training should be performed carefully. [E]

## **5. Pharmacotherapy of Diabetes Mellitus**

### **1) Insulin treatment for type 1 diabetes**

1. Treatment with multiple-dose insulin injections (prandial insulin at least 3 times/day and basal insulin 1–2 times/day) or insulin pump therapy are recommended in patients with type 1 diabetes. [A]
2. Individuals with type 1 diabetes should use insulin analogues (ultra-rapid acting insulin and basal insulin) to reduce hypoglycemia risk. [A]
3. Educating patients with type 1 diabetes is suggested to control prandial insulin dose depending on carbohydrate intake, premeal blood glucose, and anticipated activities. [E]
4. Patients with type 1 diabetes should be educated to control blood glucose by themselves in various circumstances (e.g., when they are sick, when using a steroid, and when problems occur with insulin pump). [E]
5. In patients with frequent nocturnal hypoglycemia or hypoglycemia unawareness, it is helpful to treat with a threshold-based sensor-augmented insulin pump that suspends insulin injection on low blood glucose levels. [B]

## 2) Oral agents for type 2 diabetes

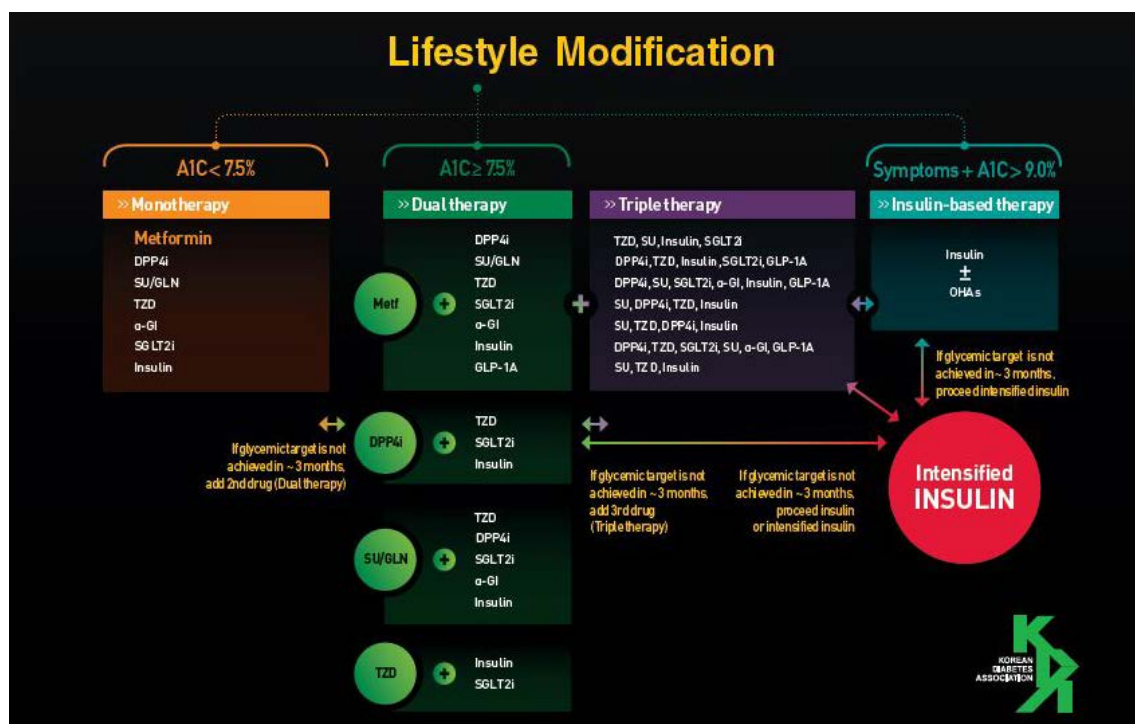
### I. Principles of Initial Therapy

1. Most patients should begin with active lifestyle changes and pharmacological therapy. [A]
2. A proper combination therapy or monotherapy should be selected considering the mechanism of action, efficacy, adverse effects, cost, characteristics of the patient, and patient preference. [E]

### II. Combination Therapy

1. Consider using metformin for the initial monotherapy pharmacological agent, or select appropriate agents depending on patient's condition. [A]
2. If monotherapy alone does not achieve the glycemic control target, select a combination therapy whose mechanism of action is different. [A]
3. Initiate a dual therapy from diagnosis, depending on patient's condition. [B]
4. Although it is possible to increase the dose of a monotherapy agent to the maximum level, it is advised to use a combination therapy at the early stage. [B]
5. In the case of combination therapy of two or more agents, choose the therapy type considering the mechanism of action of different agents, interaction, cost, and compliance. [C]
6. If the combination therapy fails, insulin therapy is suggested. However, addition of or change to other class agents can be considered. [C]

### Therapy algorithm for the initial diagnosis of type 2 diabetes



- Set the A1C target to <6.5%. If lifestyle modification does not attain this goal, consider metformin for oral hypoglycemic agent.

- Patients can begin with a dual therapy if their A1C is  $\geq 7.5\%$  at diagnosis. The combination of agents should be determined according to patient's condition and different mechanisms of action for thorough glucose control.
- Preferentially consider presence of domestic clinical data, frequently prescribed agents, and adverse effects (e.g., increase in body weight, hypoglycemia) for the arrangement of agents. Insulin therapy can be initiated from the beginning if A1C value is  $\geq 9.0\%$  at diagnosis and severe symptoms of hyperglycemia are diagnosed.
- If the pharmacological therapy combined with lifestyle modification does not achieve the glycemic control target within 3 months, blood glucose should be actively controlled by proceeding to the next stage (yellow arrow).



### **3) Injectable drugs for type 2 diabetes: insulin and GLP-1 analogues**

#### **I. Indications for Insulin Therapy**

1. If patients fail to achieve the glycemic control target with an appropriate oral hypoglycemic agent treatment, initiate insulin therapy. [A]
2. If diabetes is accompanied by metabolic dysfunction or severe hyperglycemia, patients can begin insulin therapy at diagnosis. [C]
3. Adapt the insulin therapy in cases of myocardial infarction, stroke, acute disease, or surgery. [B]

#### **II. Choosing the Insulin Therapy**

1. Prescribe basal insulin therapy, twice-daily premixed insulin therapy, or multiple insulin injection depending on the patient's condition. [B]
2. A combination therapy using oral hypoglycemic agent and insulin can be prescribed according to the patient's condition. [A]

#### **III. GLP-1 analogues**

1. GLP-1 analogues can be combined with an oral hypoglycemic agent or basal insulin. [A]

#### **4) Surgical treatment of type 2 diabetes**

1. Bariatric surgery is considered in patients who meet all the following conditions:

1-1. Aged 18-65 years [B]

1-2. Patients with type 2 diabetes with BMI  $\geq 35$  kg/m<sup>2</sup> [B] or

Patients with type 2 diabetes with BMI  $\geq 30$  to  $< 35$  kg/m<sup>2</sup> [E]

1-3. Preserving considerable pancreatic beta cell function [E]

1-4. Patients who understand the purpose of the surgery, have the correct motivations for the surgery, are willing to comply with taking nutritional supplements (e.g., calcium, vitamins), and are able to follow-up regularly after surgery [B]

## **6. Immunization**

1. Patients with diabetes are advised to receive an annual influenza vaccination. [B]
2. Pneumococcus vaccination is recommended for patients with diabetes. [C]

## **7. Management of Hypoglycemia**

1. Individuals at risk for hypoglycemia should be asked about hypoglycemia symptoms (symptomatic and asymptomatic hypoglycemia) at each encounter, and should be trained for prevention and treatment methods. [C]
2. Individuals who are aware of their hypoglycemia should consume carbohydrate that contains glucose (15–20 g) 15 minutes after treatment. If the blood glucose test shows continued hypoglycemia, the treatment should be repeated. [E]
3. In case of individuals who are unaware of their severe hypoglycemia, 20–50 mL of glucose solution (glucose 10–25 g) should be administered in 1 to 3 minutes. [E]
4. Hypoglycemia unawareness or one or more episodes of severe hypoglycemia should trigger reevaluation of the treatment regimen. [E]
5. Ongoing assessment of cognitive function is suggested with increased vigilance for hypoglycemia by the clinician, patient, and caregivers if low cognition or declining cognition is found. [A]

## 8. Management of Hypertension

1. Patients with diabetes should measure blood pressure at every routine visit. [B]
2. People with diabetes should be treated to a systolic blood pressure goal of < 140 mm Hg, and a diastolic blood pressure goal of < 85 mm Hg. [B]
3. Patients with blood pressure > 120/80 mm Hg should be advised on lifestyle changes to reduce blood pressure. [B]
4. The lifestyle modification should include diet and exercise. Patients with diabetes and hypertension should reduce sodium intake, increase potassium intake, minimize alcohol intake, and increase physical activity. [B]
5. Patients with diabetes and hypertension with a systolic blood pressure of  $\geq 140$  and/or a diastolic blood pressure  $\geq 85$  mm Hg should, in addition to lifestyle therapy, have prompt initiation of pharmacological therapy. [A]
6. Preferentially choose to prescribe either an angiotensin-converting enzyme Inhibitor or an angiotensin II receptor blocker, which is a renin-angiotensin-aldosterone system blocker, as a first-line agent for blood pressure control. [A]
7. If the first-line agent is not adequate to control blood pressure, a multiple drug therapy using agents with different mechanisms is recommended. For the agents of multiple drug therapy, calcium channel blockers are known to be more effective in preventing cardiovascular disease than are diuretics. [B]
8. If angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, or diuretics are used, serum creatinine or potassium levels should be monitored. [E]

## 9. Management of Dyslipidemia

1. It is recommended to measure the blood lipid profile (total cholesterol, HDL cholesterol, triglyceride, and LDL cholesterol) in patients with diabetes at initial diagnosis, and at least once a year thereafter. [E]
2. Intensive lifestyle modification should be advised for patients with dyslipidemia. [A]
3. Dyslipidemia should be aggressively treated in patients with type 2 diabetes. The first priority of dyslipidemia treatment is to lower LDL cholesterol to < 100 mg/dL. [A]
4. For patients with diabetes who suffer from or are at high risk for cardiovascular disease, it is recommended to lower LDL cholesterol to < 70 mg/dL. [B]
5. If the maximal tolerated dose of statin does not achieve the lipid target, a reduction in LDL cholesterol to 30–40% from the baseline is an alternative therapeutic goal. [B]
6. Statin is the first-choice agent to treat dyslipidemia of patients with diabetes. [B]
7. It is recommended to maintain HDL cholesterol at  $\geq 40$  mg/dL in men and at  $\geq 50$  mg/dL in women, and triglycerides at < 150 mg/dL. [C]

## 10. Antiplatelet Agent

1. Consider antiplatelet therapy with 100 mg/day of aspirin as a primary prevention strategy for atherosclerotic cardiovascular disease (ASCVD) in patients with type 2 diabetes who are at increased risk (10-year risk > 10%). [E]
2. In type 2 diabetic patients with multiple other risk factors (10-year risk 5–10%), consider aspirin therapy based on clinical judgment. [E]
3. Aspirin should not be recommended as a primary prevention strategy for patients with diabetes at low ASCVD risk (10-year risk < 5%), such as men aged <50 years and women aged < 60 years. [C]
4. Use aspirin therapy (100 mg/day) as a secondary prevention strategy for patients with type 2 diabetes and a history of cardiovascular disease. [A]
5. For type 2 diabetic patients with cardiovascular disease and an aspirin allergy, clopidogrel (75 mg/day) should be used. [B]
6. Dual antiplatelet therapy including aspirin is reasonable for up to a year after an acute coronary syndrome. [B]

## **11. Smoking Cessation**

1. Smoking cessation is strongly advised for all patients with diabetes. [A]
2. Smoking cessation counseling and other forms of treatment are included as a routine component of diabetes care. [B]
3. If a patient is willing to stop smoking, evaluate the preferred methods of smoking cessation and begin counseling. If a patient is unwilling to stop smoking, initiate special programs to educate on the necessity of smoking cessation and hazards of smoking or to encourage quitting smoking. [B]

## **12. Diabetes Self-Management Education**

1. Diabetes self-management education should be delivered by an educator who obtained qualification through professional training and continuous education. [A]
2. Patients with diabetes should receive standardized self-management education both at diagnosis and as needed thereafter. [B]
3. Diabetes self-management education is helpful for blood glucose control in terms of cost-saving and efficiency. [E]
4. The goals of diabetes self-management education are effective self-management and improving quality of life. The education outcome should be measured and evaluated. [C]
5. Because emotional health helps to control blood glucose and prevent complications, psychosocial care should be included in diabetes self-management education. [C]
6. Diabetes self-management education is also suitable for the people in the high-risk groups for diabetes. Diabetes can be prevented or delayed if education, support, and behavioral change are maintained. [C]



### **13. Management for Special Situations**

1. Patients need to maintain insulin and an antihyperglycemic agent when sick. However, the insulin dose needs to be adjusted. [A]
2. Sick patients are advised to check blood glucose more frequently, drink water to prevent dehydration, and maintain appropriate glucide (carbohydrates). [B]
3. If hyperglycemia persists due to acute disease, or it is difficult to eat due to loss of appetite, patients are advised to see their doctor. [E]
4. Hospitalization may be required if high fever continues, urine ketone is strongly positive, or blood glucose level is  $\geq 350$  mg/dL. [E]
5. Patients should be educated concerning the sick-day management of diabetes at the initial diagnosis. The management method should be periodically evaluated. [E]
6. Patients should be counseled about detecting and avoiding hypoglycemia during driving. [E]

## **CHAPTER 3. DIABETIC COMPLICATIONS**

### **1. Assessment and Treatment of Risk Factors of Cardiovascular Disease**

#### **I. Assessment Risk Factors of Cardiovascular Disease**

1. Because patients with type 2 diabetes are at high risk for cardiovascular disease, it is important to evaluate risk factors of cardiovascular disease and prevent such disease. [A]

1-1. Assessment must be conducted for the risk factors of cardiovascular disease as follows.

A. Sex, age, blood pressure, smoking, family history of coronary artery disease (men aged < 45 years, women aged < 55 years), and dyslipidemia (total cholesterol, HDL cholesterol, triglyceride, and LDL cholesterol) [A]

B. Abdominal obesity [B]

1-2. A variety of assessment tools such as the Framingham Risk Score or UK Prospective Diabetes Study Risk Engine can be used to assess the degree of risk of cardiovascular disease. [B]

#### **II. Screening Tests for Cardiovascular Disease**

1. In asymptomatic patients, routine screening for coronary artery disease is not recommended [A]; however, screening tests can be considered for special cases. [E]
2. Exercise stress testing is recommended for screening for coronary artery disease. If it is impossible for the individual to perform exercise, myocardial single photon emission computed tomography (SPECT) or cardiac computed tomography (CT) can be conducted. [E]

#### **III. Screening Test for Peripheral Arterial Disease (PAD)**

1. Because asymptomatic PAD commonly develops into type 2 diabetes, history taking, visual inspection, and palpation should be carefully completed. [A]
2. Ankle-brachial index (ABI) testing is the preferred screening test for PAD. [C]

#### **IV. Treatment of Cardiovascular Disease**

1. Patients with cardiovascular disease are recommended to use aspirin, statin [A], and angiotensin-converting enzyme (ACE) inhibitor. [C]
2. Using a beta blocker for at least 2 years is suggested for patients with a history of myocardial infarction. [B]

## **2. Screening and Treatment of Diabetic Nephropathy**

### **I. General Principles**

1. Blood glucose and pressure must be optimally controlled to inhibit development and progression of diabetic nephropathy. [A]
2. Urinary albumin excretion and estimated glomerular filtration rate should be monitored at diagnosis and at least once a year thereafter in patients with diabetes. [E]

### **II. Treatment and Monitoring**

1. Either an ACE inhibitor or an angiotensin II receptor blocker is recommended for the treatment of modestly elevated (30-299 mg/24 h) and higher levels of urinary albumin excretion ( $\geq 300$  mg/24 h), except in pregnancy. [A]
2. An ACE inhibitor or an angiotensin receptor II blocker is not recommended for the primary prevention of diabetes in patients who have normal blood pressure and normal urinary albumin excretion. [B]
3. Periodical monitoring of serum creatinine and potassium levels is recommended for the development of increased creatinine or potassium when ACE inhibitors, angiotensin II receptor blockers, or diuretics are used. [E]
4. For patients with diabetic nephropathy, excessive restriction of dietary protein intake ( $\leq 0.8$  g/kg/day) is not recommended. [A]
5. Continue monitoring urinary albumin excretion to assess the response to treatment and progression of the disease. [E]
6. When estimated glomerular filtration rate is  $< 60$  mL/min/1.73 m<sup>2</sup>, evaluate and manage potential complications of chronic kidney disease. [E]
7. Promptly refer to a physician experienced in the care of kidney disease for uncertainty about the etiology of kidney disease, difficult management issues, and rapidly progressing kidney disease. [B]

### **3. Screening and Treatment of Diabetic Neuropathy**

#### **I. General Principles**

1. All people with diabetes should be assessed for diabetic peripheral neuropathy starting at diagnosis of diabetes and periodically thereafter. [A]
2. Patients should follow strict glycemic control to prevent or delay the progression of diabetic neuropathy. Symptomatic treatment of diabetic peripheral neuropathy [B] and autonomic neuropathy reduce pain and improve quality of life. [E]

#### **II. Screening Test**

1. Assessment of diabetic peripheral neuropathy should include 10-g monofilament test, tuning fork test, pinprick, and ankle reflexes. [E]
2. Electrophysiological testing may be conducted for screening when the clinical features of diabetic peripheral neuropathy are atypical. [E]
3. Patients with advanced disease and cardiac autonomic neuropathy should be assessed for resting tachycardia and orthostatic hypotension on standing. [E]

## **4. Screening and Treatment of Diabetic Retinopathy**

### **I. General Principles**

Glycemic control and blood pressure control should be optimized to reduce the risk or slow the progression of diabetic retinopathy. [A]

### **II. Screening Test**

1. Patients with diabetes should undergo a comprehensive eye examination at the time of the diagnosis of diabetes. [B]
2. Patients with diabetes should have comprehensive eye examinations periodically after the initial eye examination. If there is no evidence of retinopathy in examinations, it is recommended to conduct the examinations every 2 years. [B]
3. If retinopathy is progressing or severe, then refer to ophthalmologist or optometrist and perform examinations more frequently. [B]
4. Retinal photograph is a useful screening tool for retinopathy, and it must be interpreted by a trained eye care provider. [E]
5. Women with preexisting diabetes who are planning pregnancy or who have become pregnant should receive fundus examination. Such patients should be counseled on the risk of development and/or progression of diabetic retinopathy. Fundus examination should occur in the first trimester, and then patients should be monitored during the entire pregnancy and for 1 year postpartum. [B]

### **III. Treatment**

1. For patients with macular edema, severe non-proliferative diabetic retinopathy, or proliferative diabetic retinopathy, prompt referral to a retina specialist is recommended. [A]
2. Laser photocoagulation therapy is indicated to reduce the risk of vision loss in patients with high-risk proliferative diabetic retinopathy, clinically severe macular edema, and in some cases, severe non-proliferative diabetic retinopathy. [A]
3. The presence of retinopathy is not a contraindication to aspirin therapy for cardioprotection, and aspirin does not increase the risk of retinal hemorrhage. [A]
4. Conduct treatment with antivascular endothelial growth factor for diabetic macular edema. [A]

## 5. Diabetes and Foot Care

### I. General Principles

1. Perform a comprehensive foot evaluation including lower extremity inspection and pulse examination in the legs and feet each year to identify risk factors for ulcers and amputations. [B]
2. Provide general foot self-care education to all patients with diabetes. [B]
3. A multidisciplinary approach is recommended for high-risk patients with foot ulcers, especially those who have a history of previous ulcers or amputation. [B]
4. Consider special surveillance and active management for patients who smoke or who have a history of previous lower extremity complications, loss of protective sensation, or structural abnormalities. [C]

### II. Screening Test

1. Assess patient history for claudication and pedal pulses to screen for peripheral arterial disease (PAD). Because many patients with PAD are asymptomatic, consider performing ankle-brachial index screening. [C]
2. Patients with symptoms of severe claudication or abnormal ankle-brachial index ( $\leq 0.9$ ) should receive further vascular assessment. Exercise, pharmacotherapy, and surgery can be considered. [C]

The risk of ulcers or amputations is increased in people who have the following risk factors:

- History of foot ulcer
- History of amputation
- Peripheral neuropathy
- Foot deformities
- Peripheral arterial disease
- Visual impairment
- Diabetic nephropathy (especially patients on dialysis)
- Poor glycemic control
- Cigarette smoking

Patients should be educated about appropriate foot management as follows:

- Check your feet every day. Look at blisters, open wounds, toenails, and red spots. If you cannot see the bottom of your feet, ask someone for help. Contact your doctor immediately if you discover any problems.

- Protect your feet. Wear comfortable shoes that fit well. Ask your podiatrist for special shoes. Keep your feet clean.
- Wash your feet every day and do not put your feet up for a long time. Do not put your feet into hot water. Check the water temperature before washing your feet. Rub a thin coat of skin lotion over your feet, but not between your toes.
- Protect your feet from damage made by a toenail clipper or razor blade. Trim your toenails straight across and file the edges with a nail file. Do not trim or cut calluses and corns with razor blades, and ask your healthcare provider to treat these spots.

## **6. Cancer Screening of Patients with Diabetes**

1. Patients with type 2 diabetes should be encouraged to undergo recommended age-appropriate cancer screenings. [A] Perform the screening test for cancers of the liver, pancreas, colon/rectum, breast, and bladder more frequently than recommended for the same age group. [A]
2. Patients with type 2 diabetes are advised to manage their weight, increase physical activity, quit smoking, and avoid heavy alcohol use for cancer prevention. [A]



## **CHAPTER 4. SPECIAL CASES OF DIABETES**

### **1. Treatment of Acute Diabetic Complications**

1. There is a high suspicion for diabetic ketoacidosis (DKA) and hyperosmolar hyperglycemic status (HHS) if diabetic patients have problems in general physical condition. If either DKA or HHS is diagnosed, precipitating factors must be sought. [E]
2. DKA and HHS are medical emergencies that require treatment and monitoring for multiple metabolic abnormalities and vigilance for complications. [E]
3. If the patient is severely dehydrated and unconscious, open the airway, administer intravenous (IV) normal saline, and transfer the patient to a nearby emergency room. [E]

## **2. Glycemic Control in Hospitalized Patients or Patients with Severe Diseases**

### **I. General Principle of Hyperglycemia Control in the Hospital**

1. Proper glycemic control in the hospital improves outcomes of disease treatment for patients admitted to the hospital. [B]
2. Check whether the patient record states that the patient has diabetes or no previous history of diabetes. Consider performing an A1C on patients with diabetes if not performed in the prior 3 months. [E]
3. Blood glucose testing should also be considered even though the patient is not diagnosed with diabetes if the patient has a disease or condition that may cause hyperglycemia (e.g., high-dose steroid treatment, enteral nutrition, total parenteral nutrition, octreotide, immunosuppressive drug) [C]
4. A1C testing can be considered if hyperglycemia is shown during hospitalization in patients who are not diagnosed but at risk of diabetes. [E]
5. Monitor the risk of hypoglycemia caused by strict glycemic control. [A]
6. For patients who were not diagnosed with diabetes but developed hyperglycemia during hospitalization, consider establishing an appropriate plan for follow-up testing at discharge. [E]

### **II. Hyperglycemia Control in Patients with Severe Underlying Disease**

1. Insulin therapy should be initiated through IV insulin infusions starting at a threshold of  $\geq 180$  mg/dL, and a target glucose range of 140-180 mg/dL should be maintained. [A]
2. Less stringent glucose goals may be appropriate for patients with diseases such as terminal cancer or limited life expectancy. [E]

### **III. Hyperglycemia Control in Noncritically ill Patients**

1. Initiate treatment for glycemic control for patients who were not diagnosed with diabetes, but in whom hyperglycemia was identified and continued during hospitalization. [E]
2. Maintain premeal blood glucose to  $< 140$  mg/dL and random plasma glucose to  $< 180$  mg/dL. [B]
3. A basal plus bolus correction insulin regimen is the preferred treatment for noncritically ill patients with poor oral intake or those who are not ingesting by mouth. [A]

### **3. Diabetes and Pregnancy (Gestational Diabetes Mellitus)**

1. The glycemic control target for gestational diabetes mellitus (GDM) is premeal  $\leq 95$  mg/dL, 1-hour postprandial  $\leq 140$  mg/dL, or 2-hour postprandial  $\leq 120$  mg/dL. [E]
2. Thorough glycemic control helps to reduce perinatal and obstetric complications. [B]
3. Medical nutrition therapy is a key for GDM control. Calorie intake or nutrition requirement during pregnancy must be met. Pregnancy calories should be calculated on the basis of body weight and adjusted considering the increase in body weight. [E]
4. A low-carbohydrate diet (carbohydrate 50%; protein 20%; fat 30%) improves postprandial blood glucose and helps to prevent overgrowth of the fetus. [B]
5. Light physical activity (e.g., 20–30 min walking two to three times per week) helps glycemic control and prevents overgrowth of the fetus. In the absence of contraindications (e.g., pregnancy-induced hypertension, premature rupture of membranes, preterm labor, incompetent cervix, vaginal bleeding, intrauterine growth restriction), such physical activity should be advised for all women with GDM. [E]
6. If medical nutrition therapy or exercise therapy does not achieve the glycemic target, initiate insulin therapy. [B]
7. Self-monitoring of blood glucose is critical for GDM. Focus should be given to postprandial glucose control more than fasting or premeal glucose control. [B]

#### **4. Diabetes in Older Adults**

1. While the glycemic targets for older adults are similar to those developed for younger adults, the targets should be individualized considering physical or cognitive function, or life expectancy. However, hypoglycemia or hyperglycemia leading to symptoms of acute complications should be avoided in all patients. [E]
2. Particular attention should be paid to the adverse effects or interaction of antihyperglycemic agents. [E]
3. Treatment of cardiovascular risk factors other than hyperglycemia should be determined on the basis of the benefits and the patient's condition. The treatment goals are not different from those of younger adults. [E]
4. Screening for diabetes complications should be individualized in older adults, with a focus on complications that would lead to functional impairment. [E]
5. Evaluate overall functions and reflect on treatment using the concept of geriatric syndromes, such as visual/hearing impairment, malnutrition, sarcopenia, urinary incontinence, walking difficulty, cognitive function, physical function, and polypharmacy. [E]