Staging of type 2 diabetes mellitus

S.L. Wu

Department of Cardiology, Renmin Hospital of Wuhan University, Wuhan, China

Corresponding author: S.L. Wu
E-mail: wusonglin222@163.com

Received May 19, 2014
Accepted October 27, 2014
Published March 20, 2015
DOI http://dx.doi.org/10.4238/2015.March.20.22

ABSTRACT. There is currently no reported staging system for type 2 diabetes mellitus. Here, I attempted to stage type 2 diabetes mellitus in order to help clinicians, patients, and other interested individuals to effectively evaluate patient conditions.

Key words: Type 2 diabetes mellitus; Stage of disease

There is currently no reported staging system for type 2 diabetes mellitus. Here, I attempted to stage type 2 diabetes mellitus to help clinicians, patients, and other interested individuals to effectively evaluate patient conditions. Staging may be helpful in the management of diabetes and could favorably affect health outcomes of patients with diabetes. However, the staging of type 2 diabetes requires revision, and long-term outcome studies are necessary to validate the criteria.

Type 2 diabetes can be classified into five clinical stages:

Stage 1: Pre-diabetes. This group includes patients in the following conditions: a fasting plasma glucose (FPG) level of 100-125 mg/dL (5.6-6.9 mM) (impaired fasting glucose), 2-hour plasma glucose (PG) level on oral glucose tolerance test (OGTT) 140-199 mg/dL (7.8-11.0 mM) (impaired glucose tolerance), a hemoglobin A1c (HbA1c) level of 5.7-6.4% (Genuth et al., 2003; Sacks et al., 2011). In the stage, we are irrespective of comorbidities such as hypertension, dyslipidemia, or overweight.
Stage 2: Diabetes with no complications. This group includes patients with a FPG level of $\geq 126$ mg/dL (7.0 mM), 2-h PG level on OGTT of $\geq 200$ mg/dL (11.1 mM), HbA1C level of $\geq 6.5\%$, classic symptoms of hyperglycemia, or a random PG level of $\geq 200$ mg/dL (11.1 mM) (Reaven, 1988; Expert Committee on the Diagnosis and Classification of Diabetes Mellitus, 1997; Genuth et al., 2003; American Diabetes Association, 2010). These patients may or may not have insulin resistance or classic symptoms of hyperglycemia.

Signs of insulin resistance or conditions associated with insulin resistance include acanthosis nigricans, hypertension, dyslipidemia, polycystic ovary syndrome, or small for gestational age birth weight (Genuth et al., 2003).

Stage 3: Diabetes with mild complications. This group includes patients with mild complications, including microalbuminuria and mild diabetic retinopathy (such as microaneurysms, mild hemorrhages) (Ciulla et al., 2003; Levey et al., 2003). Patients may or may not have hyperglycemia or higher or normal levels of fasting and 2-h plasma insulin or proinsulin or C-peptide on OGTT (Chiasson et al., 2002; Nathan et al., 2007).

Stage 4: Diabetes with absolute insulin deficiency. This group includes patients with hyperglycemia, and absolute insulin deficiency which is based on clinical and/or laboratory evidence. Patients may have mild to moderate complications such as diabetic nephropathy without kidney failure or diabetic retinopathy without proliferative diabetic retinopathy (PDR) (Ciulla et al., 2003; Fong et al., 2004; KDOQI, 2007).

Laboratory evidence includes levels of fasting plasma insulin or proinsulin or C-peptide lower than the normal lower limit on laboratory’s measurement method, or levels of 2-h plasma insulin or proinsulin or C-peptide during OGTT $< 5$ times of patient’s levels of fasting plasma insulin or proinsulin or C-peptide. In addition, the ratio of fasting glucose to insulin or proinsulin or C-peptide, or of 2-h PG to insulin or proinsulin or C-peptide on OGTT (Sacks et al., 2011) may be considered.

Clinical evidence: In order to achieve desired glycemic goals, the optimal treatment is insulin therapy.

Stage 5: Diabetes with serious complications. This group includes patients with serious complications including hyperglycemic crises, as well as microvascular and macrovascular complications. Patients may have hyperglycemia, as well as higher or lower or normal levels of fasting plasma insulin or proinsulin or C-peptide.

Diabetic ketoacidosis (DKA) and hyperosmolar hyperglycemic state (HHS) are the two most serious acute metabolic complications in diabetes. The diagnostic criteria for DKA include plasma glucose level of $> 250$ mg/dL, arterial pH of $< 7.30$, serum bicarbonate level of $< 18$ mEq/L, and positivity for urine ketone and serum ketone. The diagnostic criteria for HHS include plasma glucose level of $> 600$ mg/dL, arterial pH of $> 7.30$, serum bicarbonate level of $> 18$ mEq/L, effective serum osmolality of $> 320$ mOsm/kg, and stupor/coma (Kim, 2007; Kitabchi et al., 2009).

Microvascular complications include retinopathy (neovascularization and vitreous or preretinal hemorrhage), nephropathy, neuropathy (sensory, including history of foot lesions, and autonomic, including sexual dysfunction and gastroparesis), and cardiomyopathy, and macrovascular complications include coronary heart disease, cerebrovascular disease, proliferative diabetic retinopathy, peripheral arterial disease, amputation, and foot ulceration (Genuth et al., 2003; Sacks et al., 2011).

A summary of the staging for type 2 diabetes is shown in Table 1.
Table 1. Staging of type 2 diabetes mellitus.

<table>
<thead>
<tr>
<th>Stages/ Description</th>
<th>Blood glucose and insulin analysis</th>
<th>Clinical manifestation</th>
<th>Goals/Interventions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 1 Pre-diabetes</td>
<td>FPG 100-125 mg/dL (5.6-6.9 mM) [IFG], OR 2-h PG on OGTT 140-199 mg/dL (7.8-11.0 mM) [IGT], OR HbA1C 5.7-6.4%</td>
<td>With or without other diseases such as hypertension, dyslipidemia, and overweight</td>
<td>Decreasing the rate of onset of diabetes</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Basic interventions (diabetes education, medical nutrition therapy, exercise, and monitoring of the level of glycemic control), treatment of comorbidities.</td>
</tr>
<tr>
<td>Stage 2 Diabetes with no complications</td>
<td>HbA1c ≥6.5%, OR FPG ≥126 mg/dL (7.0 mM), OR 2-h PG on OGTT ≥200 mg/dL (11.1 mM), OR a random plasma glucose ≥200 mg/dL (11.1 ≥200 mg/dL (11.1 mM) in a patient with classic symptoms of hyperglycemia or hyperglycemic crisis</td>
<td>With or without classic symptoms of hyperglycemia or signs of insulin resistance</td>
<td>Glycemic control and prevention of diabetic complications</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Basic interventions, treatment of other diseases, glucose-lowering drug treatment (oral glucose-lowering agents, maybe insulin).</td>
</tr>
<tr>
<td>Stage 3 Diabetes with mild complications</td>
<td>Hyperglycemia and/or higher or normal levels of fasting plasma insulin or proinsulin or C-peptide</td>
<td>Microalbuminuria, mild diabetic retinopathy (microaneurysms, mild hemorrhages)</td>
<td>Glycemic control and delay of diabetic complications</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Basic interventions, treatment of other diseases, monitoring of complications, glucose-lowering drug treatment (oral glucose-lowering agents, maybe insulin).</td>
</tr>
<tr>
<td>Stage 4 Diabetes with absolute insulin deficiency</td>
<td>Hyperglycemia and absolute insulin deficiency based on clinical and/or laboratory evidence</td>
<td>Mild to moderate complications (such as diabetic neuropathy without kidney failure; diabetic retinopathy without PDR)</td>
<td>Glycemic control and delay/treatment of diabetic complications</td>
</tr>
<tr>
<td></td>
<td>Levels of fasting plasma insulin or proinsulin or C-peptide lower than the normal lower limit on laboratory’s measurement method, OR levels of 2-h plasma insulin or proinsulin or C-peptide during OGTT &lt;5 times of patient’s levels of fasting plasma insulin or proinsulin or C-peptide</td>
<td></td>
<td>Basic interventions, treatment of other diseases, monitoring of complications, glucose-lowering drug treatment (including insulin oral glucose-lowering agents and insulin)</td>
</tr>
<tr>
<td>Stage 5 Diabetes with serious complications</td>
<td>Hyperglycemia and/or higher, lower, or normal levels of fasting plasma insulin or proinsulin or C-peptide</td>
<td>Hyperglycemic crises: diabetic ketoacidosis, the hyperosmolar hyperglycemic state Microvascular: nephropathy, retinopathy (neovascularization, vireous or preretinal hemorrhage), neuropathy (sensory, including history of foot lesions and autonomic, including sexual dysfunction and gastroparesis), cardiomypathy macrovascular: CHD, cerebrovascular disease, peripheral arterial disease, amputation and foot ulceration</td>
<td>Glycemic control and delay/treatment of diabetic complications</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Basic interventions, treatment of other diseases, monitoring and treating complications, glucose-lowering drug treatment (oral glucose-lowering agents, maybe insulin).</td>
</tr>
</tbody>
</table>

FPG = fasting plasma glucose; IFG = impaired fasting glucose; IGT = impaired glucose tolerance; OGTT = oral glucose tolerance test; PG = plasma glucose; PDR = proliferative diabetic retinopathy; CDH = coronary heart disease.
REFERENCES