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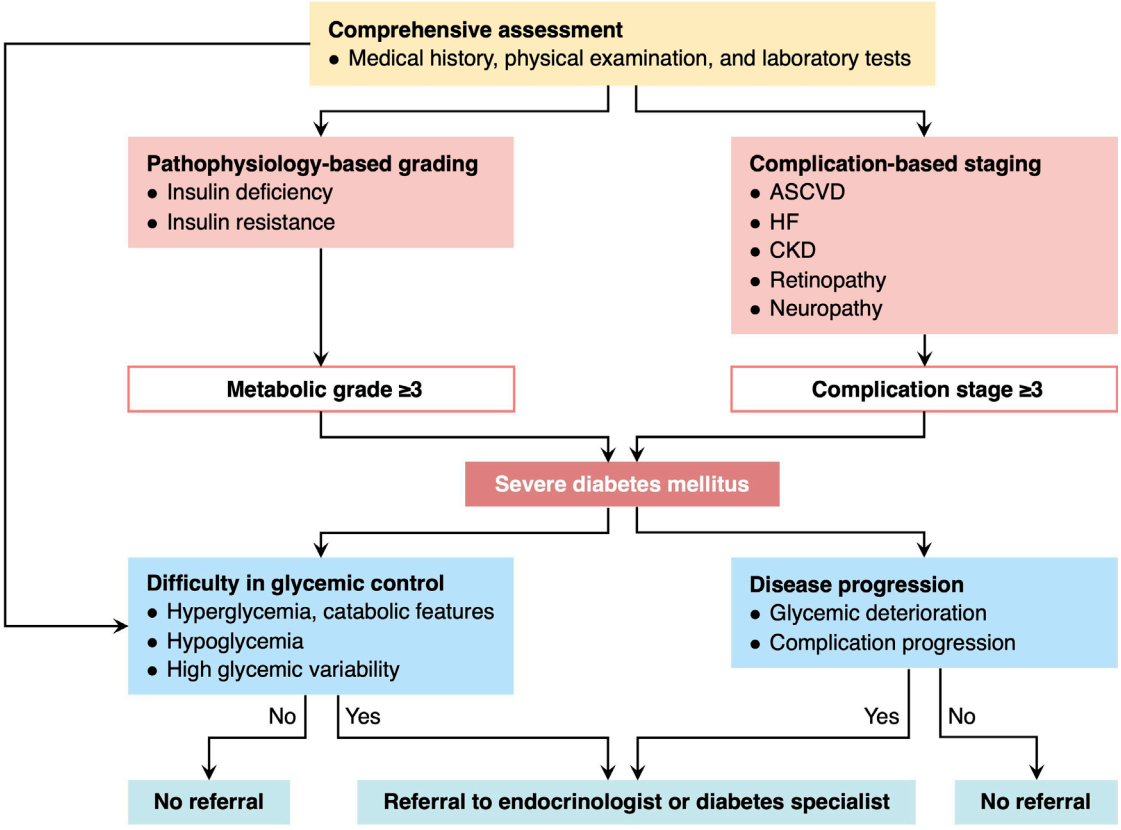

Highlights

- **We propose the Diabetes Grade–Stage Classification (DGSC) to define diabetes severity.**
- **Grading quantifies metabolic dysfunction driven by insulin deficiency and resistance.**
- **Staging reflects the cumulative burden of target organ damage across multiple systems.**
- **Severe diabetes corresponds to a metabolic grade ≥3 or a complication stage ≥3.**
- **DGSC provides a unified framework for risk stratification and precision management.**

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Defining Severe Diabetes Mellitus: A Consensus Framework for Grading and Staging Diabetes Based on Pathophysiology and Complications

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Diabetes mellitus comprises a heterogeneous group of metabolic disorders differing in etiology, clinical course, and outcomes. Traditional classifications, such as type 1 and type 2 diabetes mellitus, fail to capture the full heterogeneity, including variation in insulin deficiency, insulin resistance, and complication burden. To address these limitations, we propose the Diabetes Grade–Stage Classification, an integrated system that combines pathophysiology-based grading with complication-based staging. Grading quantifies metabolic dysfunction through the assessment of insulin deficiency and insulin resistance. In parallel, staging assesses the extent of target organ damage, particularly in the cardiovascular, renal, ocular, and nervous systems. Together, this framework enables a comprehensive assessment of disease status, identification of vulnerable or high-risk phenotypes, and implementation of risk-adapted management strategies. Clinically, it facilitates personalized care, promotes collaborative coordination, and strengthens physician–patient communication. Furthermore, this framework provides a scalable structure for integrating disease severity into both individual- and population-level interventions. Although the current criteria for grading and staging are based on expert consensus and selected clinical indicators, such as low C-peptide levels and advanced complications, further validation and refinement are needed. In conclusion, the grading and staging system provides an operational tool for classifying the severity of diabetes mellitus and has the potential to extend life expectancy and improve quality of life for people living with diabetes mellitus.

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INTRODUCTION

Diabetes mellitus is a group of metabolic disorders characterized by chronic hyperglycemia, with diverse etiologies and clinical courses [1]. Current classification distinguishes type 1 diabetes mellitus, typically resulting from autoimmune β-cell destruction, from type 2 diabetes mellitus, driven by combined insulin resistance and progressive β-cell dysfunction. However, these broad categories fail to adequately represent the wide spectrum of disease severity [2,3]. For instance, a patient newly diagnosed with mild hyperglycemia and no complications differs markedly from an individual with long-standing, poorly controlled diabetes mellitus and multi-organ involvement, despite both being classified under type 2 diabetes mellitus.

No universally accepted framework currently exists for systematically evaluating or clearly communicating disease progression in diabetes mellitus. Clinical terms, such as severe or brittle diabetes mellitus, are occasionally used to indicate high glycemic excursions or complexity in management, but they lack standardized, generally accepted definitions [4,5]. This ambiguity hampers risk stratification, development of personalized interventions, and efficient allocation of healthcare resources.

In contrast, several other chronic conditions benefit from well-established severity classification systems. For example, in oncology, tumor staging and histological grading are used to determine prognosis and guide therapeutic decisions [6]. Similarly, cardiologists employ structural and functional criteria to classify atherosclerotic cardiovascular disease (ASCVD) and heart failure (HF) [7,8], and nephrologists utilize markers, including estimated glomerular filtration rate (eGFR) and albuminuria, to stratify the severity of chronic kidney disease (CKD) [9]. These systems integrate objective indices to assess current disease status and predict clinical outcomes.

Recent advances in diabetes classification have utilized data-driven clustering analyses to identify distinct subtypes of adult-onset diabetes mellitus, such as severe insulin-deficient diabetes (SIDD) and severe insulin-resistant diabetes (SIRD). Notably, SIDD demonstrates a stronger link to retinopathy, while SIRD is more commonly associated with nephropathy [10]. However, these novel subgroups remain largely limited to research settings, as they require complex datasets and are not yet applicable to clinical practice [10-12].

To address this gap, we propose an integrated dual-axis framework for the comprehensive assessment of diabetes severity. This system combines grading, which quantifies the degree of underlying metabolic dysfunction, with staging, which reflects the extent of target organ damage. This dual-axis approach parallels established classification schemes in other fields, providing a structural foundation for risk stratification, clinical management, and health policy development. Developed by the Severe Diabetes Mellitus Task Force of the Korean Diabetes Association (KDA), this consensus statement outlines the rationale for our proposed classification, defines the operational criteria for each axis, and illustrates its clinical relevance.

RATIONALE FOR THE SEVERITY FRAMEWORK

Heterogeneity of diabetes mellitus and limitations of current classification

The current classification system for diabetes mellitus oversimplifies the substantial heterogeneity observed in clinical manifestations and disease progression [1]. Even within type 2 diabetes mellitus, clinical courses vary widely, ranging from individuals who maintain near-normal glycemia over many years to those who rapidly progress to insulin dependence and complications. Recent large-scale cohort and genetic studies further highlight these limitations. Phenotypic markers identified at diagnosis, such as age, body mass index (BMI), β-cell functional reserve, and insulin resistance, have demonstrated predictive value not only for glycemic trajectories but also for the risk of microvascular and macrovascular complications [10,13-15]. Moreover, genome-wide association studies have revealed that individuals with similar glycemic profiles can harbor significantly different genetic predispositions to complications [16,17]. These findings underscore the critical role of genotype–phenotype interactions in shaping long-term prognosis [18].

Despite these insights, their clinical application remains challenging. Patients are still primarily classified as having either type 1 or type 2 diabetes mellitus, with no standardized approach to denoting disease severity or clinical complexity. Although current guidelines recommend individualized treatment based on complications, glycosylated hemoglobin

(HbA1c), body weight, and the risk of hypoglycemia, they do not provide a unified framework for assessing overall disease severity [19,20]. There is a need for a systematic and clinically actionable framework that encompasses the full spectrum of diabetes severity, facilitates risk-adapted care, and optimizes healthcare resource allocation.

Lessons from other chronic diseases

Other chronic conditions already utilize structured severity classification systems to guide prognosis and inform treatment decisions. In HF, for instance, severity staging by the American College of Cardiology (ACC) and the American Heart Association (AHA) stratifies patients from at-risk to advanced disease, thereby guiding therapeutic intensity and timing [8]. Similarly, CKD staging, based on eGFR and albuminuria, enables effective risk stratification and individualized treatment [9]. Although these frameworks are often referenced in diabetes management, diabetes mellitus itself lacks a comprehensive severity classification that incorporates both metabolic dysfunction and complication burden.

This gap hinders the precise assessment of disease status and the implementation of tailored treatment strategies. Although diabetes care frequently employs organ-specific tools, such as retinopathy grading systems, CKD staging, or neuropathy assessments, they remain isolated and fail to capture the multisystem complexity and metabolic heterogeneity of diabetes mellitus [21-24]. Drawing inspiration from the tumor–node–metastasis (TNM) classification in oncology, a unified system for diabetes mellitus could integrate diverse clinical and biochemical data within a structured framework. Such an approach would enhance prognostic accuracy, guide therapeutic decision-making, and improve care coordination at both the individual and population levels.

PATHOPHYSIOLOGY-BASED GRADING OF DIABETES MELLITUS

The proposed framework begins with pathophysiology-based grading, which evaluates the underlying metabolic dysfunctions that drive dysregulation in carbohydrate metabolism and contribute to disease progression. Placing this assessment first establishes, a logical, causal sequence: fundamental metabolic defects serve as the engine of the disease, ultimately leading to the cumulative organ damage reflected in staging [25,26]. This approach stratifies diabetes severity into four metabolic grades based on these two core domains—insulin deficiency and insulin resistance—each representing a distinct pathophysiological mechanism either independently or in combination [27]. The term metabolic grade underscores that insulin-centric abnormalities constitute the principal determinants of metabolic dysregulation in diabetes mellitus, distinct from the broader concept of metabolic dysfunction applied to conditions such as metabolic syndrome or metabolic dysfunction-associated steatotic liver disease.

Capturing metabolic dysfunction

While the cumulative impact of diabetes mellitus on target organ systems is critical, ongoing metabolic dysfunction remains a key determinant of future risk and clinical complexity. Persistent metabolic dysregulation, stemming from insulin deficiency or insulin resistance, increases the likelihood of complications, accelerates disease progression, and often necessitates more intensive management [28]. Consequently, individuals with a similar burden of complications may exhibit markedly different degrees of metabolic disturbance and prognosis [29]. Therefore, a comprehensive severity framework should quantify both insulin deficiency and insulin resistance to accurately assess the pathophysiological basis of diabetes mellitus.

To reflect these pathophysiological principles, we propose an insulin-centric framework. For example, β-cell function can be assessed by C-peptide levels [30] or the homeostasis model assessment 2 of β-cell function (HOMA2-B) [31], whereas insulin resistance can be estimated by the homeostasis model assessment 2 of insulin resistance (HOMA2-IR) [31] in patients not using insulin, or by daily insulin requirements [32] in those receiving insulin therapy. The HOMA indices were developed to estimate β-cell function and insulin resistance, assuming an intact liver–pancreas axis and a stable metabolic state [31,33,34]. Although reference values for these indices have been suggested [35-37], clinically validated cut-points are not yet universally established, and their accuracy at the individual level is limited [38]. In clinical settings where biochemical markers are not readily available, clinicians may estimate metabolic grade using clinical indicators. For example, marked obesity, reflected by BMI or waist circumference, elevated triglycerides, or the requirement for high doses of insulin sensitizers (e.g., metformin or thiazolidinediones) suggest substantial insulin resistance, whereas long disease duration or a lean phenotype in type 2 diabetes mellitus may indicate predominant insulin deficiency.

In light of these limitations, we propose that suggested indices should be serve as supportive, not definitive, indicators of metabolic dysfunction, with final judgment based on a comprehensive clinical assessment. To facilitate clinical application, provisional criteria derived from existing literature are summarized in Supplementary Table 1. These criteria are intended to guide, rather than determine, diagnostic decisions and will require further validation across diverse populations.

Insulin deficiency

Insulin secretory capacity is estimated by measuring C-peptide levels. Although stimulation tests are the gold standard, non-fasting C-peptide measurements obtained within 5 hours after eating, when measured alongside blood glucose, correlate closely with stimulated C-peptide levels from a mixed meal tolerance test [39] and can serve as a practical alternative [3,30]. Low non-fasting C-peptide levels (<200 pmol/L) indicate severe insulin deficiency [3] and are associated with greater glycemic variability and hypoglycemia risk, particularly in insulin-treated patients [40]. HOMA2-B can also be used to assess insulin secretion. The spectrum of insulin deficiency ranges from preserved β-cell function, through progressive β-cell dysfunction, to β-cell failure [31,35].

Insulin resistance

For individuals treated with insulin, the total daily insulin dose (TDD) is a meaningful measure of insulin resistance. Typical insulin requirements for people with type 1 diabetes mellitus are approximately 0.5 to 0.6 U/kg/day, but these values vary substantially in type 2 diabetes mellitus [32]. However, TDD can also be affected by concomitant medications that modify insulin sensitivity (e.g., metformin or thiazolidinediones) or alter endogenous insulin secretion (e.g., sulfonylureas and dipeptidyl peptidase-4 inhibitors). In those not receiving insulin therapy, HOMA2-IR can be used to assess insulin resistance. A high TDD or HOMA2-IR value significantly exceeding the typical range indicates marked insulin resistance, as observed in individuals with obesity or insulin antibodies [32,38].

Metabolic grades

The integration of insulin deficiency and insulin resistance defines four metabolic grades (Table 1). Clinicians should recognize that insulin deficiency and insulin resistance may be discordant within an individual, necessitating separate evaluation of each to accurately define the overall metabolic grade.

Grade 1: mild metabolic dysfunction

Grade 1 is characterized by mild insulin deficiency and mild insulin resistance. Individuals in this grade are typically managed with lifestyle modification [41], with or without oral antidiabetic medications, and are at low risk of metabolic decompensation.

Table 1. Pathophysiology-based metabolic grading of diabetes mellitus: definitions and proposed criteria

Grade	Definition	Insulin deficiency[a]	Insulin resistance[b]
1. Mild metabolic dysfunction	Mild insulin deficiency, mild insulin resistance	Non-fasting C-peptide >600 pmol/L (1.8 ng/mL)[c] or mild impairment of β-cell function	TDD <0.4 U/kg/day or mild impairment of insulin sensitivity
2. Moderate metabolic dysfunction	Moderate insulin deficiency, moderate insulin resistance	Non-fasting C-peptide 200–600 pmol/L (0.6–1.8 ng/mL)[c] or moderate impairment of β-cell function	TDD 0.4–0.9 U/kg/day or moderate impairment of insulin sensitivity
3. Severe metabolic dysfunction	Marked insulin deficiency, severe insulin resistance	Non-fasting C-peptide 80–200 pmol/L (0.24–0.6 ng/mL)[c] or severe impairment of β-cell function	TDD 1.0–1.9 U/kg/day or severe impairment of insulin sensitivity
4. Very severe metabolic dysfunction	Near-complete insulin deficiency, extreme insulin resistance	Non-fasting C-peptide <80 pmol/L (0.24 ng/mL)[c] or very severe impairment of β-cell function	TDD ≥2.0 U/kg/day or very severe impairment of insulin sensitivity

Each pathophysiological domain can be graded independently according to its specific criteria.
TDD, total daily insulin dose.
[a]Assessment may be based on indices such as non-fasting C-peptide or homeostasis model assessment 2 of β-cell function (HOMA2-B); cutoff values for these measures have been proposed in previous studies [3,30,35], [b]Assessment may be based on indices such as TDD or homeostasis model assessment 2 of insulin resistance (HOMA2-IR); cutoff values for these measures have been proposed in earlier research [32,36-38], [c]Measured within 5 hours after eating.

Grade 2: moderate metabolic dysfunction

Grade 2 encompasses moderate insulin deficiency and moderate insulin resistance. Management typically requires multiple oral antidiabetic medications or low-dose basal insulin [42,43]. Individuals in this grade experience increased glycemic excursions.

Grade 3: severe metabolic dysfunction

Grade 3 includes marked insulin deficiency or severe insulin resistance. Intensive management, often involving basal-plus or basal-bolus insulin regimens, is typically required [19,20]. Individuals in this grade are at increased risk for both uncontrolled hyperglycemia and hypoglycemia.

Grade 4: very severe metabolic dysfunction

Grade 4 indicates β-cell failure (near-complete insulin deficiency) or extreme insulin resistance. Individuals in this grade are at risk for hyperglycemic crises (diabetic ketoacidosis [DKA] and hyperosmolar hyperglycemic state) [44] and severe hypoglycemia [45]. Management may require automated insulin delivery (AID) systems [46,47]. In selected cases, pancreatic islet transplantation can be considered [48].

COMPLICATION-BASED STAGING OF DIABETES MELLITUS

Complementing pathophysiologic grading, complication-based staging categorizes diabetes severity by the presence and extent of target organ damage. This assessment encompasses critical domains commonly affected by chronic hyperglycemia, including ASCVD, HF, CKD, retinopathy, and neuropathy (Fig. 1) [7,8,21-23]. These stages reflect a continuum, progressing from at-risk status to advanced, irreversible, and life-threatening complications. Although progression from stage 1 to stage 4 generally correlates with diabetes duration and prior glycemic control, the staging system also incorporates the cumulative effects of other major risk factors, such as hypertension, dyslipidemia, and overweight or obesity [49]. This pragmatic framework succinctly summarizes overall disease burden, facilitating clinical decision-making. Table 2 outlines the staging criteria, illustrative clinical findings, and corresponding management implications. Notably, staging can be applied independently to each affected organ system, enabling a detailed, organ-specific evaluation of disease severity.

Stage 1: at risk

Individuals in stage 1 exhibit no clinical evidence of diabetes-related complications but have established cardiometabolic risk factors for future organ damage, such as age ≥55 years, hypertension, dyslipidemia, and overweight or obesity. At this early stage, clinical management should focus on risk factor modification and preventive care [50].

Stage 2: subclinical disease

Stage 2 includes individuals with early or asymptomatic target

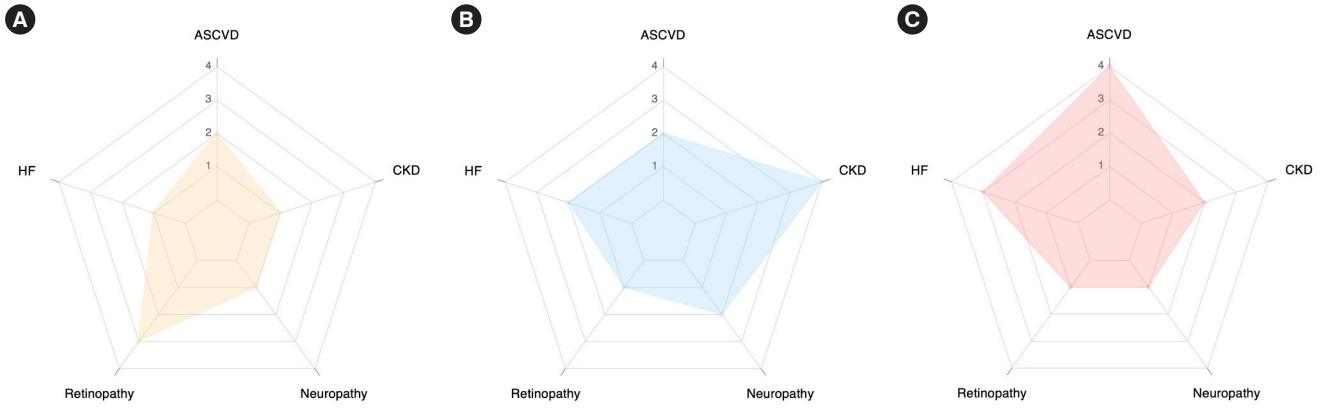

Fig. 1. Heterogeneity of complication profiles in people with diabetes mellitus. (A, B, C) Radar charts depicting diverse complication profiles for three hypothetical patients. Each axis represents a major domain of diabetes-related complications: atherosclerotic cardiovascular disease (ASCVD), heart failure (HF), chronic kidney disease (CKD), retinopathy, and neuropathy. Severity within each domain is scored from 1 (at risk) to 4 (advanced disease). The resulting polygons illustrate the distinct and heterogeneous burden of target organ damage, demonstrating that patients with the same type of diabetes mellitus can present with markedly different clinical phenotypes. These findings underscore the value of complication-based staging in capturing individual disease burden.

Table 2. Complication-based staging of diabetes mellitus: definitions, examples, and clinical implications

Stage	Definition	Representative clinical findings	Clinical implications
1. At risk	No clinical evidence of complications, but presence of established cardiometabolic risk factors	Age ≥55 years, hypertension, dyslipidemia, overweight or obesity	Emphasis on risk factor modification and preventive care
2. Subclinical disease	Early or asymptomatic target organ involvement identified through screening	Subclinical ASCVD, pre-HF, CKD stage 1 or 2 with albuminuria (30–300 mg/g), NPDR without DME, asymptomatic neuropathy	Proactive screening and early intervention to prevent progression
3. Clinical disease	Overt, symptomatic, or functionally limiting complications affecting target organs	Stable angina, symptomatic HF, cerebral large or small vessel disease, PAD with claudication, CKD with albuminuria (>300 mg/g) or CKD stages 3 to 5 not yet requiring renal replacement therapy, NPDR with DME or non-high-risk PDR, symptomatic neuropathy	Multidisciplinary care to address established complications
4. Advanced disease	Irreversible, disabling, or life-threatening complications indicating extensive target organ damage	ACS, advanced HF, ischemic stroke, CLTI, ESKD, high-risk PDR or significant vision loss, disabling neuropathy	Comprehensive, interprofessional management of advanced complications

Each organ system can be staged independently to reflect its domain-specific complication severity.
ASCVD, atherosclerotic cardiovascular disease; HF, heart failure; CKD, chronic kidney disease; NPDR, non-proliferative diabetic retinopathy; DME, diabetic macular edema; PAD, peripheral artery disease; PDR, proliferative diabetic retinopathy; ACS, acute coronary syndrome; CLTI, critical limb-threatening ischemia; ESKD, end-stage kidney disease.

organ involvement, typically identified through routine screening. Examples include subclinical ASCVD, pre-HF, preserved eGFR with low-grade albuminuria (30 to 300 mg/g), non-proliferative diabetic retinopathy (NPDR) without macular edema, and asymptomatic neuropathy. Early identification at this stage allows for timely intervention to halt or slow disease progression [20].

Stage 3: clinical disease

Stage 3 is characterized by overt, symptomatic, or functionally limiting complications affecting major organs. Clinical manifestations include stable angina, symptomatic HF, peripheral artery disease with claudication, CKD with albuminuria (>300 mg/g) or CKD stages 3 to 5 not yet requiring renal replacement therapy (RRT), NPDR with macular edema or non-high-risk proliferative diabetic retinopathy (PDR), and symptomatic neuropathy. This stage typically requires multidisciplinary management to control established complications and improve quality of life [51].

Stage 4: advanced disease

Stage 4 represents irreversible, disabling, or life-threatening complications, reflecting extensive systemic involvement. Representative conditions include acute coronary syndrome, ischemic stroke, critical limb-threatening ischemia, advanced HF (ACC/AHA stage D), end-stage kidney disease requiring RRT, high-risk PDR or significant vision loss, and disabling neuropathy. At this stage, comprehensive, interprofessional management is essential [52].

THE DIABETES GRADE–STAGE CLASSIFICATION: INTEGRATING METABOLIC GRADING AND COMPLICATION STAGING

Building on established definitions of metabolic grades and complication stages, we introduce a two-dimensional matrix, the Diabetes Grade–Stage Classification (DGSC), to conceptualize diabetes severity (Fig. 2). The horizontal axis denotes metabolic grade (grades 1–4), while the vertical axis represents complication stage (stages 1–4). Progression along the horizontal axis indicates worsening metabolic dysfunction, whereas movement along the vertical axis reflects increasing complication burden. The DGSC enables simultaneous assessment of metabolic grade and complication stage, thereby capturing the heterogeneous, multidimensional nature of diabetes severity.

Dynamic nature and practical implications

The DGSC provides a comprehensive view of diabetes severity by integrating the current degree of metabolic dysfunction and

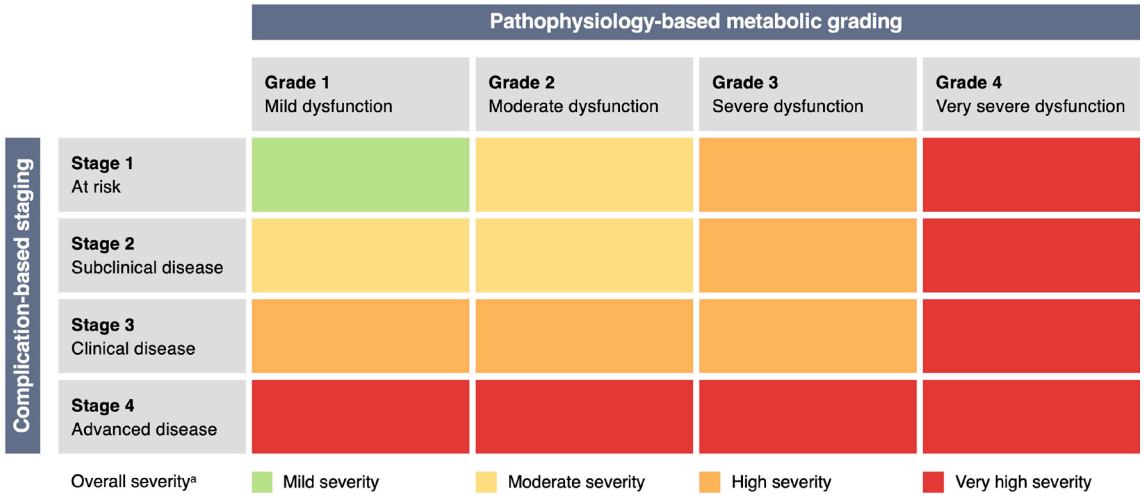

Fig. 2. The Diabetes Grade–Stage Classification (DGSC): Integrated severity matrix for diabetes mellitus. A two-dimensional matrix conceptualizing overall diabetes severity by integrating pathophysiology-based grading (horizontal axis, grades 1–4) and complication-based staging (vertical axis, stages 1–4). The horizontal axis reflects progressive metabolic dysfunction, whereas the vertical axis represents the increasing burden of cumulative target organ damage. The color gradient from green (mild severity) to red (very high severity) qualitatively depicts the combined disease burden. The DGSC provides a holistic framework for classifying distinct clinical phenotypes and facilitating risk-adapted management strategies. [a]Although color intensity qualitatively indicates overall severity, each metabolic domain is graded separately according to defined criteria, and each organ system is staged independently to reflect domain-specific complication burden.

cumulative burden of chronic complications. In stable circumstances, this matrix offers a clinically meaningful snapshot to guide therapeutic intensity and inform risk stratification. However, diabetes severity is inherently dynamic. Severity may improve with lifestyle modification or pharmacologic intervention [53,54], whereas deterioration may result from progressive loss of β-cell function [55-57] or worsening insulin resistance [58]. For example, individuals initially classified as grade 2, stage 3 may achieve better glycemic control by improving insulin sensitivity through weight loss, despite persistent complications. Conversely, those with grade 4, stage 2 may experience rapid progression of complications if timely management is not instituted. Moreover, transient factors affecting glycemic control, such as intercurrent illness or concomitant treatment, may also alter an individual's disease status [59,60]. Therefore, periodic reassessment of both metabolic grade and complication stage is crucial to adjust therapeutic strategies and improve outcomes.

Relationship to traditional classification of diabetes mellitus

The DGSC is intended to complement, not replace, the conventional classification of diabetes mellitus. The traditional system classifies diabetes mellitus based on underlying etiology, such as type 1, type 2, specific types, and gestational diabetes mellitus [2,3]. This etiologic framework remains essential for guiding fundamental aspects of diabetes care, including decisions regarding lifelong insulin therapy and screening for complications [3,61]. However, it does not provide information about the current severity of the disease or the complexity of management, both of which may differ markedly among individuals with the same type of diabetes mellitus.

The DGSC addresses this limitation by introducing two additional dimensions: metabolic grading and complication staging. By combining these systems, clinicians and researchers can describe diabetes mellitus more comprehensively. For example, rather than simply noting 'type 2 diabetes mellitus,' one might specify 'type 2 diabetes mellitus with grade 2 insulin deficiency, grade 3 insulin resistance, stage 3 HF, and stage 3 CKD.' This expanded description clarifies multiple aspects of the current disease status, thereby providing a more precise and actionable perspective.

GRADE–STAGE PHENOTYPES: CLINICAL SCENARIOS

The DGSC delineates distinct clinical phenotypes in diabetes mellitus, each with specific implications for management. The

following scenarios highlight the diverse presentations encountered in clinical practice and illustrate how the grade–stage matrix can support personalized care.

Low grade, low stage: low metabolic and complication burden

Individuals classified as grade 1 or 2 and stage 1 or 2 typically exhibit both mild-to-moderate metabolic dysfunction and a low burden of complications. This group often includes those with recent-onset type 2 diabetes mellitus who achieve adequate glycemic control through lifestyle modification or oral antidiabetic medications, as well as individuals with longer disease duration but few, if any, complications and only moderate metabolic impairment. β-Cell function is generally preserved, insulin resistance is mild, and there is little or no evidence of target organ damage. Management focuses on maintaining individualized glycemic targets, addressing cardiometabolic risk factors, and regular screening for complications [20,50].

High grade, low stage: predominant metabolic severity

Some individuals with diabetes mellitus exhibit severe metabolic dysfunction despite the absence or near absence of diabetic complications. For example, a young adult presenting with newly diagnosed type 1 diabetes mellitus and DKA would be categorized as grade 4, stage 1. Similarly, a person with longstanding type 2 diabetes mellitus and obesity, requiring high insulin doses but demonstrating low-stage complications, fits this phenotype. Such cases may be underestimated by frameworks that focus solely on diabetes complications, yet they require intensive management to address the risk associated with severe metabolic dysfunction [19,20].

Low grade, high stage: prominent complication severity

In contrast, some individuals with diabetes mellitus may develop advanced complications despite relatively stable metabolic parameters. Consider an older adult with a two-decade history of type 2 diabetes mellitus who has survived a myocardial infarction and is now on RRT but maintains adequate glycemic control with a low dose of insulin. This patient would be classified as grade 2, stage 4. Although metabolic indices may appear well controlled, the substantial burden of target organ damage necessitates comprehensive, multidisciplinary care, with an emphasis on secondary prevention and cardiometabolic protection [49].

High grade, high stage: dual burden of metabolic dysfunction and complications

Patients with both grade 4 metabolic dysfunction and stage 4 complications represent those with the greatest therapeutic challenge and highest risk of acute and chronic diabetes-related events. This group includes individuals with recurrent hospitalizations for acute metabolic decompensation, advanced HF due to ischemic heart disease, blindness, or a history of kidney transplantation [62]. Such patients require intensive, multidisciplinary or interprofessional management [52]. Application of the DGSC in this population facilitates recognition of clinical complexity, supports the development of individualized care plans, and enhances coordination among healthcare providers.

CLINICAL CONSIDERATIONS FOR THE DGSC

We define severe diabetes mellitus, according to the DGSC, as a metabolic grade of 3 or higher or a complication stage of 3 or higher. After identifying severe diabetes mellitus using the DGSC, we recommend a secondary clinical evaluation to determine whether to refer the patient to a specialist or intensify treatment beyond the current regimen. This decision is based primarily on two considerations: difficulty in glycemic control (e.g., persistent or marked hyperglycemia with or without catabolic features, recurrent or severe hypoglycemia, or high glycemic variability) and the degree or rate of disease progression (e.g., worsening glycemic control or advancing complications), as outlined in the clinical pathway (Fig. 3).

Difficulty in glycemic control

This represents a composite assessment of ongoing metabolic instability. It includes persistent or marked hyperglycemia with or without catabolic features (unintentional weight loss or ketosis [with or without ketoacidosis]), recurrent or severe hypoglycemia, and high glycemic variability, as measured by continuous glucose monitoring or frequent self-monitoring of blood glucose [19,20]. These clinical features, which indicate failure to achieve stable glycemic control, strongly suggest that a patient may require specialized care.

Disease progression

This factor assesses whether the patient's condition is currently worsening. Evidence of progression includes glycemic deterio-

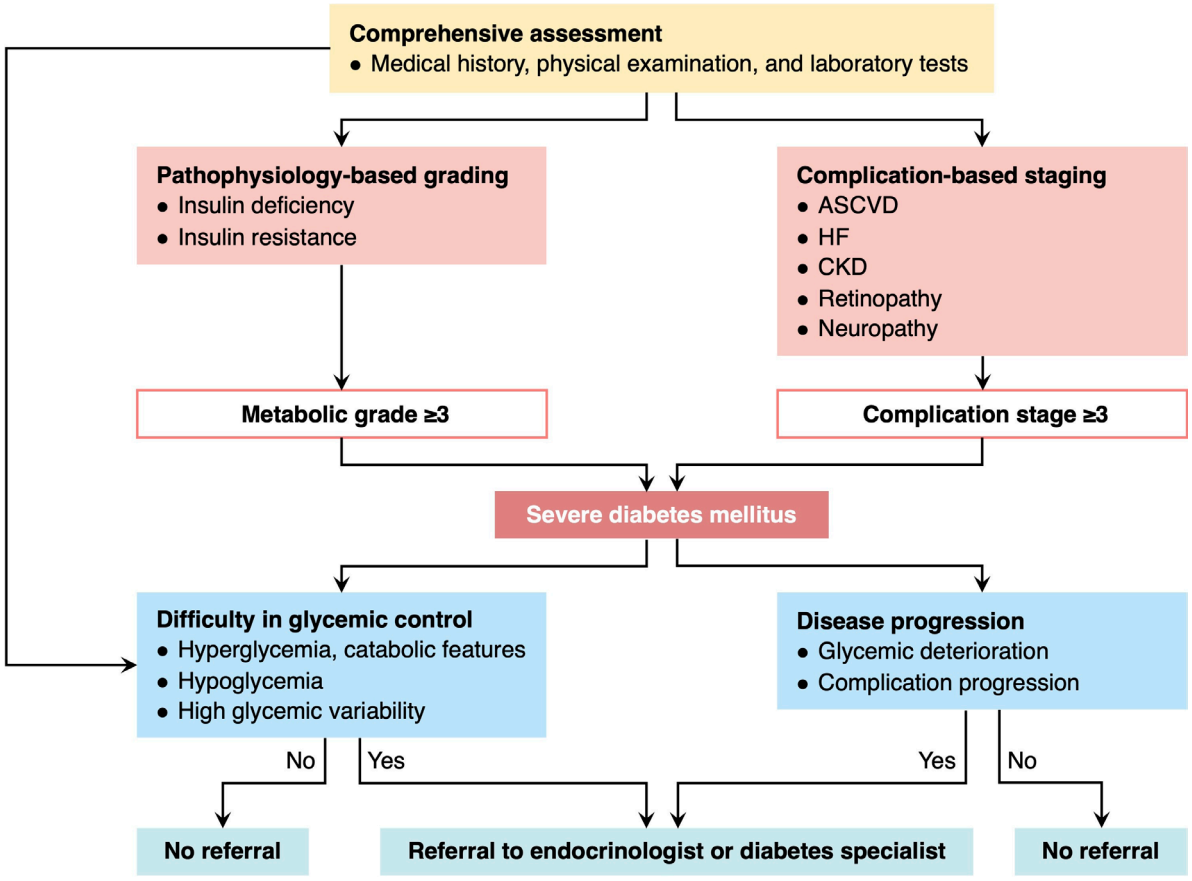

Fig. 3. Clinical pathway for comprehensive assessment and specialist referral. Flowchart depicting the proposed clinical decision-making process. Comprehensive assessment, including medical history, physical examination, and laboratory tests, feeds into two parallel evaluation pathways: pathophysiology-based grading (insulin deficiency and insulin resistance) and complication-based staging (atherosclerotic cardiovascular disease [ASCVD], heart failure [HF], chronic kidney disease [CKD], retinopathy, and neuropathy). Patients with a metabolic grade ≥3 or a complication stage ≥3 are classified as having severe diabetes mellitus. For these patients, a secondary assessment determines the need for specialist referral, guided by two key factors: difficulty in glycemic control (hyperglycemia, catabolic features, hypoglycemia, and high glycemic variability) and evidence of disease progression (glycemic deterioration and complication progression). Significant challenges in either area warrant referral to an endocrinologist or diabetes specialist.

ration, such as a rising HbA1c despite treatment adjustments, or complication progression, such as advancing retinopathy, worsening albuminuria, or declining eGFR. Such progression signals that the current management strategy is insufficient to halt the disease course [63].

The presence of significant challenges in either component—difficulty in glycemic control or evidence of disease progression—should prompt referral to an endocrinologist or diabetes specialist for advanced management. It is important to emphasize that such referral is intended to complement, not replace, the essential care provided by other subspecialists (e.g., cardiologists or nephrologists) for patients with advanced complications. Glycemic management in the setting of severe organ damage is inherently complex and is best achieved through coordinated, multidisciplinary, and interprofessional care. Conversely, patients with high-grade or high-stage disease who remain stable in both domains may be appropriate for continued management within their current care setting, with planned periodic re-evaluation.

CLINICAL AND POLICY IMPLICATIONS

Implications for clinical management

The DGSC provides a practical, risk-adapted framework for

personalized diabetes management. Assigning each patient both a metabolic grade and a complication stage allows, healthcare providers to align therapeutic intensity with disease severity and allocate resources accordingly. A key strength of this approach lies in its ability to support evidence-based, personalized decision-making at the point of care. For instance, guidelines from both the KDA and the American Diabetes Association (ADA) recommend early initiation of sodium-glucose cotransporter 2 inhibitors or glucagon-like peptide-1 receptor agonists for people with type 2 diabetes mellitus and established ASCVD or CKD [19,20], which correspond to complication stage 3 or 4 in our system. Similarly, patients classified as metabolic grade 4 due to severe insulin deficiency can be readily identified as candidates for advanced diabetes technologies, such as AID systems.

Both the ADA Standards of Care in Diabetes and the DGSC emphasize the importance of comprehensive risk assessment, interprofessional care, and collaborative management, particularly for patients with advanced or complex disease [50,52]. While the ADA highlights integrated assessment of comorbidities and complications, a formal structure for simultaneously evaluating both metabolic dysfunction and complication burden is not yet established. The DGSC addresses this gap by providing a standardized and interpretable framework for assessing both dimensions concurrently, thereby supporting more precise risk stratification and personalized care.

The DGSC also enhances physician–patient communication by providing a shared language to describe disease status, treatment rationale, and long-term goals. It strengthens mutual understanding, supports engagement and adherence, and promotes shared decision-making [64]. While international societies emphasize person-centered care [24], the DGSC translates the multidimensional complexity of diabetes mellitus into actionable clinical categories.

Implications for healthcare systems and policy

At the healthcare system level, the DGSC provides a clear framework for improving health outcomes. Individuals at metabolic grade 4 or complication stage 4, those with the most severe metabolic dysfunction or highest complication burden, may be prioritized for enrollment in chronic care models and intensive management strategies [52,65]. From a policy perspective, reimbursement criteria could be linked to DGSC-defined severity, ensuring equitable access to advanced therapies [63].

Longitudinal tracking of stage and grade across populations can serve as a dynamic quality metric for healthcare systems, enabling monitoring of disease progression, evaluation of the impact of interventions, and identification of disparities in care [63]. For instance, an increase in the prevalence of stage 3 or 4 complications may prompt a review of preventive strategies, whereas a decrease could reflect successful early intervention [65,66]. On a global scale, adoption of a unified severity framework, such as the DGSC, could facilitate standardized disease reporting and meaningful international benchmarking, allowing countries to compare outcomes more reliably and share best practices, particularly in resource-limited settings [67,68]. Ultimately, this approach supports global efforts to reduce disparities in diabetes care and to advance equitable, data-driven health policy.

LIMITATIONS AND FUTURE DIRECTIONS

Despite its strengths, the DGSC has several limitations that warrant further research and refinement. First, current metabolic grading thresholds largely derive from expert consensus or limited empirical evidence. As new data accumulate, these thresholds will require validation and potential recalibration. Second, practical implementation may be constrained by the lack of standardized, widely accessible measures for metabolic dysfunction, such as C-peptide and HOMA2 indices [30,38,69]. Broader adoption will depend on developing more accurate, affordable, and standardized methods to assess metabolic dysfunction in diverse healthcare settings. Third, accurate complication staging relies on comprehensive and equitable screening for target organ damage. Incomplete assessment, especially in resource-limited settings, may lead to misclassification and undermine the benefits of the DGSC. Fourth, metabolic grade and complication stage may evolve over time. Further validation—including longitudinal analyses to determine how transitions across grades and stages reflect disease progression and treatment response, and studies evaluating whether DGSC-guided management improves outcomes—is needed to establish the clinical validity and utility of the DGSC. Finally, although incorporating grade and stage into existing classification systems may increase perceived complexity, integration with automated workflows and decision-support tools could facilitate their implementation in precision diabetes care.

CONCLUSIONS

The DGSC, integrating pathophysiology-based metabolic grading with complication-based staging, offers a precise and comprehensive framework of the severity of diabetes mellitus. By capturing both the dynamic state of metabolic dysfunction and the cumulative burden of target organ damage, the DGSC addresses a key gap left by traditional classification schemes. Its practical structure can guide risk-adapted treatment decisions, facilitate shared decision-making between patients and providers, and align healthcare resources with clinical need. As evidence accumulates, further refinement and integration into clinical practice and policy frameworks will be essential to realize its full potential. By operationalizing the concept of severity in diabetes care, the DGSC has the potential to advance precision medicine, improve long-term outcomes, and prevent complications through timely, individualized interventions.

SUPPLEMENTARY MATERIALS

Supplementary materials related to this article can be found online at https://doi.org/10.4093/dmj.2025.0739.

CONFLICTS OF INTEREST

Jae Hyun Bae has been a managing editor of the *Diabetes & Metabolism Journal* since 2024. Kyung-Soo Kim has been a associate editor of the *Diabetes & Metabolism Journal* since 2024. They were not involved in the review process of this article. Otherwise, there was no conflict of interest.

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Supplementary Table 1. Pathophysiology-based metabolic grading of diabetes mellitus: definitions and provisional criteria

Grade	Definition	Insulin deficiency [3,35]	Insulin resistance [36,37]
1. Mild metabolic dysfunction	Mild insulin deficiency, mild insulin resistance	Non-fasting C-peptide >600 pmol/L (1.8 ng/mL)[a] or HOMA2-B ≥64%	TDD <0.4 U/kg/day or HOMA2-IR <2.3
2. Moderate metabolic dysfunction	Moderate insulin deficiency, moderate insulin resistance	Non-fasting C-peptide 200–600 pmol/L (0.6–1.8 ng/mL)[a] or HOMA2-B 44%–64%	TDD 0.4–0.9 U/kg/day or HOMA2-IR 2.3–2.5
3. Severe metabolic dysfunction	Marked insulin deficiency, severe insulin resistance	Non-fasting C-peptide 80–200 pmol/L (0.24–0.6 ng/mL)[a] or HOMA2-B 30%–44%	TDD 1.0–1.9 U/kg/day or HOMA2-IR 2.6–4.0
4. Very severe metabolic dysfunction	Near-complete insulin deficiency, extreme insulin resistance	Non-fasting C-peptide <80 pmol/L (0.24 ng/mL)[a] or HOMA2-B <30%	TDD ≥2.0 U/kg/day or HOMA2-IR ≥4.1

Each pathophysiological domain can be graded independently according to its specific criteria.
HOMA2-B, homeostatic model assessment 2 estimates of β-cell function; TDD, total daily insulin dose; HOMA2-IR, homeostatic model assessment 2 estimates of insulin resistance.
[a]Measured within 5 hours after eating.