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TYPE 2 DIABETES MELLITUS: PATHOPHYSIOLOGY, DIAGNOSTICS, AND CONTEMPORARY THERAPEUTIC STRATEGIES. A REVIEW

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ABSTRACT

Type 2 diabetes mellitus (T2DM) remains one of the dominant clinical challenges in modern medicine. According to the 11th edition of the IDF Diabetes Atlas (2025), 589 million adults currently suffer from this condition, and it is estimated that by 2050, the number of patients will increase by 46%, reaching 853 million.

This paper reviews current knowledge on the pathogenesis of T2DM, which includes peripheral insulin resistance, the progressive loss of pancreatic beta-cell mass alongside secondary impairment of their secretory function, and systemic inflammation. Diagnostic criteria are presented in accordance with the 2025 PTD (Diabetes Poland) guidelines, including recommendations for screening and the identification of high-risk groups.

A fundamental part of the study is devoted to modern pharmacotherapy, with a particular focus on SGLT-2 inhibitors and GLP-1 receptor agonists as drugs with documented cardioneproprotective effects. Furthermore, the role of metabolic surgery and the importance of comprehensive, multidisciplinary care in the prevention and treatment of organ-related complications are discussed.

KEYWORDS

Type 2 Diabetes Mellitus, Insulin Resistance, SGLT-2 Inhibitors, GLP-1 Agonists, Cardiovascular Complications, Renal Complications

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1.Introduction

Type 2 diabetes mellitus is a chronic metabolic disease in which hyperglycemia results from coexisting pathomechanisms: progressive peripheral tissue resistance to insulin and the loss of pancreatic islet beta-cell function along with the reduction of their mass (Li M et al. 2022). It accounts for over 90% of diabetes cases and ranks high among the causes of premature death, severe disability, and rising healthcare expenditures.

According to the 11th edition of the IDF Diabetes Atlas (2025), the number of affected adults aged 20–79 stands at 589 million, and at the current growth rate, the projection for 2050 reaches 853 million (IDF Diabetes Atlas, 11th ed., 2025). However, it is estimated that the actual number of patients is higher due to the insidious, long-term asymptomatic course of the disease.

It is precisely this stealthy nature of the illness that causes many patients to present to a diabetologist only when advanced organ complications have already developed.

The cardiovascular risk in patients with T2DM is 2–4 times higher than in the general population: cardiovascular diseases affect approximately 32% of patients and constitute the leading cause of mortality, encompassing both macroangiopathic complications (ischemic heart disease, stroke, peripheral artery disease) and microangiopathic ones (retinopathy, nephropathy, neuropathy) (Einarson, T. R et al., 2018).

A decade of intensive clinical research has brought breakthrough discoveries in the pharmacotherapy and pathophysiology of T2DM.

This review aims to systematize current clinical knowledge, with a particular focus on new classes of drugs whose cardionephroprotective effects have secured their place in currently applicable therapeutic algorithms.

2.Materials and methods

This paper is a narrative review based on an analysis of current scientific literature regarding the pathophysiology, diagnostics, and treatment of type 2 diabetes. The review incorporates original publications, clinical trials, meta-analyses, and current guidelines from both national and international scientific societies. A literature search was conducted in the PubMed/MEDLINE, Scopus, and Web of Science databases using keywords including "type 2 diabetes mellitus," "insulin resistance," "beta-cell dysfunction," "GLP-1 receptor agonists," "SGLT2 inhibitors," and "tirzepatide."

The analysis specifically focused on papers published between 2015 and 2025, while also accounting for landmark studies of fundamental importance to the subject matter. Inclusion criteria consisted of full-text, peer-reviewed publications concerning the pathophysiological mechanisms of T2DM, therapeutic strategies, and organ-related complications of the disease. Case reports and papers with limited evidentiary value or those not subjected to a peer-review process were excluded. The gathered material underwent qualitative analysis, involving the synthesis and critical evaluation of available data, considering their clinical significance and relevance. The objective of the adopted methodology was to organize the contemporary state of knowledge in the field of type 2 diabetes and to identify key directions in the development of pharmacotherapy and clinical management strategies.

3. Pathophysiology

3.1 Insulin resistance

Skeletal muscles, the liver, and adipose tissue are the main tissues that insulin acts upon. When their response to insulin decreases, even despite its elevated plasma concentration, it is referred to as insulin resistance (Petersen, M. C et al. 2018).

The molecular basis of insulin resistance lies in the impairment of the post-receptor signaling cascade: compromised tyrosine phosphorylation of insulin receptor substrate 1 (IRS-1) results in the inhibition of the PI3K/Akt pathway and insufficient translocation of GLUT-4 to the cell membrane, which limits glucose uptake by myocytes and adipocytes (Zhao, X et al. 2023).

Visceral adipose tissue, particularly when accumulated within the abdominal cavity, plays a key role in the pathogenesis of insulin resistance. Its heightened lipolytic activity leads to an increased release of free fatty acids into the portal circulation, resulting in their excessive flux into hepatocytes. Within liver cells, serine kinases, primarily JNK and IKKβ, become activated, disrupting the proper phosphorylation of IRS-1 and impairing insulin signaling transduction, which leads to the consolidation of hepatic insulin resistance. This process is accompanied by chronic low-grade inflammation associated with the increased secretion of pro-inflammatory adipokines, such as TNF-α, IL-6, and resistin, alongside a simultaneous decrease in the concentration of adiponectin—an adipokine that exhibits anti-inflammatory effects and enhances insulin sensitivity in tissues (Szukiewicz D, 2023; Blüher M, 2020).

For many years, T2DM was explained by the concept of the "triumvirate" or rather the "ominous triumvirate," which included skeletal muscle insulin resistance, excessive hepatic glucose production, and impaired insulin secretion resulting from pancreatic β-cell dysfunction. Today, however, it is known that the situation is more complex. DeFronzo proposed the concept of the "ominous octet," expanding the previous model to include additional disorders such as increased lipolysis in adipose tissue, decreased secretion and impaired action of incretins, increased renal glucose reabsorption, dysfunction of central mechanisms regulating appetite, and excessive glucagon secretion by pancreatic alpha cells (DeFronzo, R. A et al. 2022). Each of the aforementioned mechanisms represents a distinct therapeutic target, which is why current therapeutic algorithms favor the use of drugs with complementary mechanisms of action.

3.2.Beta cells

For many years before overt hyperglycemia develops, the pancreas responds to increasing IR with a compensatory increase in insulin secretion, leading to a vicious cycle as hyperinsulinemia further reduces insulin sensitivity. However, this adaptive mechanism has its biological limits, and over time, glucose homeostasis becomes disrupted. The progressive loss of beta-cell secretory capacity, exacerbated by gluco- and lipotoxicity as well as chronic intra-islet inflammation, ultimately leads to pancreatic beta-cell dysfunction and apoptosis (Lv, C et al. 2022).

Findings regarding pancreatic beta-cell apoptosis are reflected in autopsy studies conducted on 124 cases, which found a lower relative beta-cell volume in individuals with type 2 diabetes by 40% and 41% for obese and lean individuals, respectively (Butler, A. E et al. 2003).

Hyperglycemia itself exacerbates the impairment of beta-cell function, as increased glucose availability leads to enhanced production of reactive oxygen species, primarily within the mitochondria. Beta cells are particularly susceptible to oxidative stress due to the relatively low activity of antioxidant enzymes, such as catalase and glutathione peroxidase, which limits their ability to neutralize excess reactive oxygen species. Consequently, chronic hyperglycemia can promote the accumulation of oxidative stress and progressive beta-cell dysfunction (Newsholme, P et al. 2019).

A separate and often underappreciated element of pathogenesis in clinical practice is the role of islet amyloid polypeptide (IAPP), whose deposits have been observed in a significant percentage of patients with type 2 diabetes. The IAPP polypeptide is stored and secreted alongside insulin, which, in a hyperglycemic environment, leads to its increased secretion. Its excess tends to aggregate, during which conformational changes occur, forming left-handed helical aggregates. The transitional structures formed during this process exhibit significantly increased toxicity toward beta cells by damaging cell membranes and inducing endoplasmic reticulum stress, leading to their accelerated apoptosis (Bishoyi, A. K et al., 2020).

3.3.Systemic inflamation

Elevated concentrations of hsCRP, IL-6, TNF-α, and IL-1β in patients with type 2 diabetes are not merely secondary markers of the disease but play a significant role in its development. Chronic low-grade inflammation, associated with the activation of adipose tissue macrophages and increased secretion of pro-inflammatory cytokines, leads to the deepening of insulin resistance and gradual pancreatic beta-cell dysfunction, impairing their ability to properly secrete insulin (Dludla, P. V et al. 2023). A significant role in linking metabolic disorders with the inflammatory response is attributed to the NLRP3 inflammasome. Its activation can occur, among others, under the influence of IAPP oligomers and cholesterol crystals, leading to the intensification of pro-inflammatory signaling. The literature indicates that this mechanism may constitute one of the key links connecting metabolic dysfunction with chronic activation of the immune system (Ordovas-Montanes, J. M et al. 2012).

In the last decade, the role of the gut microbiota in the pathogenesis of type 2 diabetes has become a subject of intense research. A recurring pattern of dysbiosis is observed in patients, involving, among others, a relative reduction in the abundance of bacteria such as *Bifidobacterium* and *Akkermansia muciniphila*, alongside a shift in the microbiota composition toward populations with greater pro-inflammatory potential. These changes promote the disruption of the intestinal barrier integrity, leading to increased translocation of lipopolysaccharide (LPS) into the portal circulation. The resulting phenomenon of metabolic endotoxemia, through the activation of the TLR receptor, plays a significant role in maintaining a chronic, low-grade inflammatory response, which constitutes one of the key elements in the pathogenesis of insulin resistance in T2DM (Zhou, Z et al. 2022).

3.4.The incretin axis

Following meal ingestion, L cells of the small and large intestine secrete glucagon-like peptide-1 (GLP-1), while K cells of the duodenum secrete glucose-dependent insulinotropic polypeptide (GIP). Both hormones exhibit an incretin effect, enhancing glucose-dependent insulin secretion by pancreatic β-cells. Additionally, GLP-1 inhibits glucagon secretion, slows gastric emptying, and increases the feeling of satiety, whereas GIP primarily exerts insulinotropic effects, and its influence on glucagon secretion is glucose-dependent rather than a constant inhibitory effect. In type 2 diabetes, the incretin effect is weakened primarily due to the impaired response of pancreatic β-cells to incretin signals, particularly GIP. While GLP-1 secretion is largely preserved, its insulinotropic action is partially diminished. Conversely, the response to GIP is significantly impaired regarding the stimulation of insulin secretion, which limits its physiological incretin function. Furthermore, GIP may exhibit altered effects on adipose tissue under insulin-resistant conditions, influencing lipid metabolism differently than in a physiological state. These observations formed the basis for the development of tirzepatide, a dual GIP and GLP-1 receptor agonist, which significantly improves glycemic control and metabolic parameters in T2DM patients by simultaneously activating both incretin pathways (Nauck, M. A et al. 2023).

4. Diagnosis of type 2 diabetes

4.1.Diagnosis criteria for diabetes based on the 2025 Guidelines of the Polish Diabetes Association (PTD)

The current diagnostic criteria for T2DM, formulated by the WHO and adopted by the PTD in the 2025 guidelines, are based on four equivalent biochemical methods:

1. Random plasma glucose (a sample taken at any time of day, regardless of the time of the last meal) ≥ 200 mg/dL (11.1 mmol/L) in the presence of accompanying symptoms of hyperglycemia (polyuria, polydipsia, unintended weight loss);
2. Fasting plasma glucose measured after 8–14 hours since the last meal ≥ 126 mg/dL (7.0 mmol/L), confirmed by two independent measurements;
3. Two-hour plasma glucose during an oral glucose tolerance test (OGTT) ≥ 200 mg/dL (11.1 mmol/L);
4. HbA1c ≥ 6.5% (48 mmol/mol) measured using an NGSP-certified method. *(PTD, 2025)*.

4.2.LADA, MODY

Diagnosing type 2 diabetes in an adult patient is not always accurate. LADA (latent autoimmune diabetes in adults), or slow-onset autoimmune diabetes, affects 8–10% of patients misdiagnosed with T2DM and is characterized by the presence of autoantibodies—most commonly GADA—a gradual loss of endogenous insulin secretion, and a faster progression to beta-cell failure than in classic T2DM (Mishra, R et al. 2020). Overlooking it leads to inadequate treatment with oral medications alone and accelerated progression to absolute insulin deficiency. When the medical history and clinical presentation raise doubts, C-peptide levels and a panel of diabetes autoantibodies should be measured.

Conversely, monogenic diabetes (MODY) should be considered in young patients (the median age of diagnosed patients in the UK is 20 years) who are not overweight and have a positive family history. Patients with MODY due to mutations in the *HNF1A* or *HNF4A* genes are characterized by a good clinical response to low-dose sulfonylureas. Meanwhile, patients with MODY caused by *GCK* gene mutations usually do not require pharmacological treatment (Shields, B. M. et al. 2017). These data emphasize the importance of correct MODY diagnosis, as it allows for the avoidance of inadequate or even unnecessary long-term therapy.

4.3.Screening Tests

Due to the fact that hyperglycemia is usually asymptomatic, the PTD recommends annual screening for individuals in high-risk groups. Furthermore, diabetes screening is recommended every 3 years for everyone over the age of 45. The aforementioned risk factors include: overweight, obesity, family history of diabetes (first-degree relative), low physical activity, membership in ethnic groups at high risk for diabetes, previously detected prediabetes, gestational diabetes, giving birth to a child with a birth weight > 4 kg, hypertension, dyslipidemia, polycystic ovary syndrome, and cardiovascular disease (PTD, 2025).

5.Therapeutic Strategies

5.1.Lifestyle modification

Pharmacotherapy does not waive the necessity of lifestyle modification. The DPP (Diabetes Prevention Program) study demonstrated that an intensive behavioral intervention leading to a weight reduction of ≥7%—based on a low-fat, low-calorie diet and increasing physical activity to ≥150 min/week—reduces the risk of progression from prediabetes to T2DM by 58%, which is nearly twice as effective as metformin alone (31%) (DPP Research Group, 2015).

Among various nutritional patterns, the Mediterranean diet has received particular attention—rich in olive oil, fish, legumes, and nuts, while low in red meat and highly processed carbohydrates. The PREDIMED study and subsequent analyses demonstrated that this diet reduces the risk of developing diabetes by approximately 30% compared to a control group (Jannasch, F et al. 2017).

Physical activity, including aerobic, resistance, and HIIT (High-Intensity Interval Training), constitutes a fundamental element of type 2 diabetes prevention. Physical exertion increases glucose uptake by skeletal muscles through both insulin-dependent and insulin-independent pathways. A key role in this relationship is played by AMPK (AMP-activated protein kinase), which, when activated during exercise, serves as the primary regulator of insulin-independent glucose uptake in muscles. Furthermore, aerobic training increases the activity of oxidative enzymes and mitochondrial content in skeletal muscles, leading to more efficient oxidation of glucose and fatty acids (Kirwan, J. P. et al. 2017).

5.2.Metformin

Metformin remains the first-line drug in current PTD, ADA, and EASD guidelines, which results from its favorable safety and efficacy profile: a low risk of hypoglycemia, a neutral or weight-reducing effect, affordability, and extensive long-term clinical experience (Davies, M. J. et al., 2022).

Metformin inhibits hepatic gluconeogenesis and lipogenesis by inhibiting complex I of the mitochondrial respiratory chain. This inhibition leads to the secondary activation of AMPK, which also contributes to improving peripheral tissue sensitivity to insulin. Furthermore, recent years have shown that metformin can beneficially modulate the composition of the gut microbiota (Rena, G. et al., 2017).

An additional advantage of metformin is its protective effect on the cardiovascular system. A meta-analysis of randomized clinical trials demonstrated a significant reduction in cardiovascular risk and all-cause mortality compared to control groups, further strengthening the position of metformin as a holistically acting drug in the therapy of type 2 diabetes (Zakynthinos, G. E. et al., 2026).

5.3.SGLT-2 inhibitors

Sodium-glucose cotransporter 2 (SGLT2) inhibitors act by selectively blocking glucose reabsorption in the proximal tubule of the kidney. Healthy kidneys are capable of reabsorbing up to 450g of glucose daily; however, the implementation of SGLT2 inhibitor therapy causes a decrease in glucose reabsorption efficiency to 60–80g per day. Meta-analyses of studies involving patients with type 2 diabetes indicate that the resulting glucosuria translates into a significant reduction in glycated hemoglobin (HbA1c) by an average of 0.5–0.7% (Vallon, V et al. 2017).

The EMPA-REG OUTCOME trial proved to be the breakthrough that changed clinical thinking regarding T2DM treatment. In patients with established cardiovascular disease, empagliflozin reduced the risk of the primary composite endpoint (CV death, non-fatal myocardial infarction, or non-fatal stroke) by 14% (HR 0.86; p=0.04), cardiovascular mortality by 38%, and the risk of hospitalization for heart failure by 35%—with a median follow-up of only 3.1 years (Zinman, B et al. 2015). Similar trends regarding cardiovascular benefits were observed in the CANVAS (canagliflozin) and DECLARE-TIMI 58 (dapagliflozin) trials (Packer, M et al. 2020).

The cardioprotective mechanisms of this drug class extend far beyond the glycemic effect: they include the reduction of preload and afterload, optimization of cardiomyocyte energy metabolism, and a direct decrease in glomerular hyperfiltration and intraglomerular pressure (Verma, S et al., 2018).

The 2025 PTD Guidelines recommend SGLT2 inhibitors as a priority therapy, independent of baseline HbA1c, for every T2DM patient with documented coronary artery disease (CAD), heart failure (regardless of ejection fraction), or chronic kidney disease (CKD) with an eGFR $\geq$ 20 ml/min/1.73 m². In these populations, the organ-protective benefit is substantial enough to justify the initiation of the drug even when glycemia is well-controlled (PTD, 2025).

5.4.GLP-1 agonists

Drugs in this class mimic the physiological action of endogenous GLP-1: they stimulate insulin secretion proportionally to glycemia, inhibit endogenous glucagon secretion, slow gastric emptying, and reduce appetite through a direct effect on the hunger centers in the hypothalamus (Müller, T. D. et al., 2019). The clinical effect is synergistic: in addition to reducing HbA1c, GLP-1 receptor agonist therapy also results in sustained and significant weight loss, averaging 2–7 kg (Nauck, M. A. et al., 2021).

The cardioprotective effect of GLP-1RAs has been confirmed in several independent trials with hard endpoints. The LEADER trial showed that liraglutide reduces MACE (Major Adverse Cardiovascular Events) by 13%, cardiovascular mortality by 22%, and all-cause mortality by 15% (Marso, S. P. et al., 2016). Subcutaneous semaglutide in the SUSTAIN-6 trial reduced MACE by 26% (Marso, S. P. et al., 2016), while dulaglutide in REWIND showed a reduction of 12% (Gerstein, H. C. et al., 2019).

5.5.Tirzepatide

Tirzepatide is a single molecule that activates both incretin receptors: GIP and GLP-1. Unlike classic GLP-1 agonists, the additional activation of the GIP receptor enhances the insulinotropic effect of the drug through unique synergy. The key to its effectiveness is overcoming the $\\beta$-cell resistance to GIP, which in type 2 diabetes results from chronic hyperglycemia. This mechanism works in two stages: the GLP-1 component lowers glycemia, which "unblocks" the GIP receptors, allowing them to restore the early phase of insulin secretion (Holst, J. J., & Rosenkilde, M. M 2020).

In the SURPASS program, tirzepatide (5, 10, and 15 mg/week) demonstrated significant clinical efficacy. At the highest dose of 15 mg, the drug reduced HbA_{1c} levels by an average of 2.07% while simultaneously decreasing body weight by 7–9.5 kg (Rosenstock, J et al. 2021).

The SURMOUNT program, in turn, confirmed that in an obese population without diabetes, tirzepatide at a dose of 15 mg reduces body weight by an average of 20% within 72 weeks, which represents a significant result compared to a mean weight loss of 3% in the placebo group (Jastreboff, A. M et al. 2022). These results are comparable to the bariatric effect but achieved through pharmacological means, marking a new horizon in the treatment of obesity and T2DM.

A separate, groundbreaking chapter is the SURPASS-CVOT study, published in December 2025, which is the first prospective, randomized cardiovascular trial dedicated to tirzepatide. Compared to dulaglutide—a drug with documented cardioprotection—tirzepatide reduced the composite MACE endpoint by approximately 8% and all-cause mortality by 16% over a median follow-up of four years. The study further demonstrated tirzepatide's superiority over dulaglutide regarding renal outcomes, slowing the reduction of eGFR by 3.54 ml/min/1.73m^2. This confirms that cardiovascular benefits stem from mechanisms extending beyond glycemic control and weight reduction alone (Nicholls, S. J et al. 2025).

5.6.Insulin therapy

Insulin therapy in type 2 diabetes (T2DM) is still too often delayed—a phenomenon known as clinical inertia, which affects both patients and physicians. Meanwhile, the indications for its implementation are precisely defined: severe symptomatic hyperglycemia ($HbA_{1c} > 10\%$, glycemia > 300 mg/dL), failure of maximum doses of non-insulin medications, acute conditions or illnesses exacerbating hyperglycemia, pregnancy, and newly diagnosed T2DM with massive hyperglycemia requiring rapid correction.

The preferred initiation strategy remains the BOT (basal-only therapy) regimen. It consists of adding basal insulin to existing oral therapy at a dose of 10 units/day or 0.1–0.2 units/kg of body weight.

A key element of success is patient education in self-monitoring. The first assessment of glycemia is performed within 4–5 days of starting therapy (which allows the drug to reach a steady state in the body). Subsequently, based on morning fasting glucose results, the dose is increased by 2–4 units at intervals of several days until the target glucose values are achieved and glucose metabolism is fully balanced (PTD 2025).

6.Bariatric and metabolic treatment

Bariatric surgery is not only a weight-reducing procedure; it is an effective metabolic procedure. Systematic reviews confirm that bariatric surgery leads to T2DM remission, defined as an HbA1c level < 6.5% without dedicated pharmacotherapy. The effectiveness of bariatric surgery as a metabolic therapy is higher the shorter the duration of the disease prior to the procedure; furthermore, the procedures themselves vary in effectiveness, with the Roux-en-Y gastric bypass demonstrating the highest efficacy (Balasubaramaniam, V., & Pouwels, S 2023).

According to the new definition of clinical obesity published by Rubino et al. in the Lancet in 2025, indications for metabolic surgery should consider not only BMI but also the presence of organ complications, which expands the qualification criteria (Rubino, F et al. 2025)

7. Organ-specific diabetes complications

7.1.Cardiovascular system

Cardiovascular disease is the most common cause of death in patients with T2DM. A systematic review by Einarson et al. estimated its prevalence at approximately 32% in this population. The key pathogenetic factor is the accelerated progression of atherosclerotic changes, stimulated by chronic hyperglycemia, atherogenic dyslipidemia, and arterial hypertension (Einarson, T. R. et al., 2018). Effective prevention of cardiac events requires rigorous control of the lipid profile. Therapeutic targets for LDL cholesterol levels are as follows: < 55 mg/dL for very high-risk patients, < 70 mg/dL for high-risk individuals, and < 100 mg/dL for moderate-risk cases. Equally important is the optimization of blood pressure to values below 130/80 mmHg. In antihypertensive pharmacotherapy for patients with T2DM and cardiac complications, a combination of an ACE inhibitor and a beta-blocker is preferred (PTD, 2025).

7.2.Kidneys

Diabetic kidney disease (DKD) is the leading cause of end-stage renal disease in developed countries, with estimates suggesting that DKD accounts for as much as 38% of cases (Chaudhuri A et.al 2022). SGLT-2 inhibitors are among the cornerstones of modern nephroprotection. Through the mechanism of natriuresis and the restoration of tubuloglomerular feedback, these drugs effectively reduce glomerular hyperfiltration. Consequently, they significantly limit the rate of eGFR decline and reduce the risk of progression to kidney failure and the development of cardiovascular complications. A significant advancement in therapy is the introduction of finerenone—a non-steroidal, selective mineralocorticoid receptor antagonist. Unlike classic drugs in this class, finerenone exhibits potent anti-inflammatory and anti-fibrotic effects within the renal tissue. As a result, it significantly reduces the risk of a clinically significant decrease in eGFR and lowers the incidence of cardiovascular events in patients with DKD (Tuttle, K. R et.al. 2022). Breakthrough evidence of its efficacy was provided by the FIDELIO-DKD study, which demonstrated that in patients with T2DM and chronic kidney disease, adding finerenone to standard therapy (RAA system blockade) results in an 18% reduction in the risk of the primary renal composite endpoint compared to placebo. The primary endpoint included time to kidney failure, a sustained decrease in eGFR of at least 40% from baseline, or death from renal causes. Additionally, finerenone exhibits a strong antiproteinuric effect. In the studied population, a 31% reduction in the urinary albumin-to-creatinine ratio (UACR) was observed after just 4 months of treatment (Bakris, G. L et.al. 2020).

7.3.Retinopathy

Despite widespread access to modern ophthalmological methods, diabetic retinopathy (DR) remains the dominant cause of vision loss in the adult population. The etiopathogenesis of the condition is complex, encompassing not only the classically described microangiopathy and neovascularization but also neurodegenerative processes occurring within the retina. Although laser photocoagulation remains the standard for preventing blindness, its invasive nature drives the search for alternatives. Currently, anti-VEGF injections are gaining increasing importance, despite challenges related to the need for frequent administration. However, the digitalization of medicine is becoming a breakthrough in patient care; the development of artificial intelligence allows for precise monitoring and the identification of early pathological changes, which may significantly improve patient outcomes (Wang, Z et al. 2024).

8. Discussion

Type 2 diabetes is a disease whose landscape is constantly changing—both in its biological and therapeutic dimensions. What was merely a research hypothesis a decade ago is now a standard of care: SGLT-2 inhibitors and GLP-1 agonists have ceased to be just glucose-lowering drugs, becoming the foundation of holistic heart and kidney protection, used regardless of HbA_{1c} levels. Simultaneously, the introduction of tirzepatide establishes a new benchmark for efficacy in reducing glycemia and body weight.

The pathophysiology of T2DM is multi-layered; it encompasses peripheral tissue insulin resistance, progressive dysfunction and loss of beta-cell mass, chronic inflammation, gut microbiota dysbiosis, and disturbances in the incretin axis. Effective management of this disease requires precise differential diagnosis (including LADA and MODY) and active population screening.

Ultimately, therapeutic success depends not only on the choice of a modern molecule but on the quality of care. The individualization of therapy, taking into account the cardiovascular risk profile, renal function, degree of obesity, and patient preferences, is key. A multidisciplinary approach—combining the expertise of a diabetologist, dietitian, nurse educator, and, if necessary, a podiatrist and psychologist—is not merely supportive, but a prerequisite. In this system, therapeutic education remains an integral element of treatment, without which even the most advanced pharmacotherapy will not reach its full potential.

9. Conclusions

A decade of intensive clinical research has ultimately confirmed that type 2 diabetes is not a homogeneous condition but a complex process whose pathogenesis involves a series of parallel mechanisms, each requiring a distinct therapeutic approach. Modern treatment reduced solely to rigorous glycemic control proves insufficient, as it does not provide full protection against organ complications. The introduction of new drug classes, such as SGLT-2 inhibitors and GLP-1 receptor agonists, has fundamentally changed this situation by offering cardiorenal protective benefits independent of the hypoglycemic effect, necessitating a revision of existing management algorithms. Equally important as the choice of pharmacotherapy is precise differential diagnosis; unrecognized LADA or monogenic forms of diabetes, misdiagnosed as T2DM, represent a real clinical problem leading to years of inadequate treatment. Since microangiopathic complications develop insidiously and are often advanced at the time of diagnosis, systematic screening becomes an absolute obligation rather than an option. Finally, it must be emphasized that no modern molecule can replace lifestyle modification, which invariably remains the foundation of prevention and therapy—a fact that no clinical study has yet undermined.

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