CHAPTER 9

TRIGLYCERIDE-GLUCOSE BODY MASS INDEX (TYG-BMI) AS A NON-INVASIVE MARKER FOR STRATIFYING THE RISK OF DEVELOPING METABOLIC DYSFUNCTION-ASSOCIATED STEATOTIC LIVER DISEASE (MASLD) IN PATIENTS WITH TYPE 2 DIABETES MELLITUS

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INTRODUCTION

Metabolic dysfunction-associated steatotic liver disease (MASLD), previously known as non-alcoholic fatty liver disease (NAFLD), is currently considered the most common chronic liver disease worldwide and one of the major causes of hepatocellular carcinoma[1]. The understanding of this disease has changed significantly following the international consensus reached in 2023, according to which the term NAFLD was replaced by MASLD. The new nomenclature emphasizes the leading role of metabolic dysfunction in the development of hepatic steatosis and reflects the current understanding of the disease as a systemic manifestation of metabolic disturbances rather than exclusively a local liver disorder. Although the term NAFLD has been widely used, the designation "non-alcoholic" does not fully reflect the heterogeneous aetiology of the disease. In addition, the term "fatty" has been considered potentially stigmatizing. Furthermore, some individuals with metabolic risk factors for NAFLD, particularly type 2 diabetes mellitus, may consume alcohol above the relatively strict thresholds traditionally used to define the "non-alcoholic" nature of the disease. Such patients may not be adequately captured by the existing nomenclature and have historically been excluded from some clinical trials and treatment considerations[2]. The prevalence of MASLD in the general adult population is high and continues to increase in parallel with the growing incidence of obesity, type 2 diabetes mellitus (T2DM), hypertension, and atherogenic dyslipidaemia. Patients with T2DM are at particularly high

[1] Lujan P. V., Viñas Esmel E., Meseguer E. S. Overview of Non-Alcoholic Fatty Liver Disease (NAFLD) and the Role of Sugary Food Consumption and Other Dietary Components in Its Development. Nutrients. 2021. Vol. 13, № 5. Art. 1442. DOI: 10.3390/nu13051442.

[2] Rinella M. E., Lazarus J. V., Ratziu V., Francque S. M., Sanyal A. J., Kanwal F. A multi-society Delphi consensus statement on new fatty liver disease nomenclature. Hepatology. 2023. Vol. 78, № 6. P. 1966–1986. DOI: 10.1097/HEP.0000000000000520.

risk: according to current guidelines, more than two-thirds of these patients may have MASLD, while the presence of diabetes significantly increases the risk of fibrosis progression and the development of clinically significant complications. Therefore, patients with T2DM represent a priority group for systematic assessment of the risk of progressive liver disease. Current estimates indicate that MASLD affects 38% of the global adult population[3]. The highest prevalence of MASLD is observed in people with obesity (75%) or T2DM (69%)[4] The pathogenesis of MASLD is multifactorial and involves insulin resistance, adipose tissue dysfunction, excessive influx of free fatty acids into the liver, increased de novo lipogenesis, impaired fatty acid oxidation, lipotoxicity, oxidative stress, mitochondrial dysfunction, chronic low-grade inflammation, and disturbances in interorgan metabolic communication.[5], [6] Insulin resistance is considered a key pathogenic mechanism underlying MASLD and contributes to disturbances in of carbohydrate, lipid and protein metabolism[7]. Decreased sensitivity of peripheral tissues to insulin is accompanied by increased lipolysis in adipose tissue, increased supply of free fatty acids to the liver, activation of de novo lipogenesis, impaired β-oxidation of fatty acids and accumulation of triglycerides in hepatocytes. As the disease progresses, steatosis is replaced by chronic inflammation, oxidative stress, mitochondrial dysfunction and the development of fibrosis, which significantly increases the risk of cirrhosis and hepatocellular carcinoma[8].

Despite significant progress in the study of the pathogenesis of the disease, the diagnosis of early stages of MASLD remains a difficult clinical task. Liver biopsy continues to be considered the reference method for assessing steatosis, inflammation and fibrosis, but its invasiveness, risk of complications and

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[3] Younossi Z. M., Kalligeros M., Henry L. Epidemiology of metabolic dysfunction-associated steatotic liver disease. Clin Mol Hepatol. 2025. Vol. 31, Suppl. P. S32–S50. DOI: 10.3350/cmh.2024.0431

[4] Koliaki C., Dalamaga M., Kakounis K., Liatis S. Metabolically Healthy Obesity and Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD): Navigating the Controversies in Disease Development and Progression. Curr Obes Rep. 2025. Vol. 14. Art. 46. DOI: 10.1007/s13679-025-00637-9

[5] Bansal S. K., Bansal M. B. Pathogenesis of MASLD and MASH – role of insulin resistance and lipotoxicity. Aliment Pharmacol Ther. 2024. Vol. 59, Suppl. 1. P. S10–S22. DOI: 10.1111/apt.17930.

[6] Kim B. K. Metabolic Dysfunction-Associated Steatotic Liver Disease and Obesity: Pathogenesis, Diagnostics, Risk Stratification, and Therapeutic Approach. Kaohsiung J Med Sci. 2026. Art. e70227. DOI: 10.1002/kjm2.70227.

[7] Miller D. M., McCauley K. F., Dunham-Snary K. J. Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD): Mechanisms, Clinical Implications and Therapeutic Advances. Endocrinol Diabetes Metab. 2025. Vol. 8, № 6. Art. e70132. DOI: 10.1002/edm2.70132.

[8] Truong X. T., Lee D. H. Hepatic Insulin Resistance and Steatosis in Metabolic Dysfunction-Associated Steatotic Liver Disease: New Insights into Mechanisms and Clinical Implications. Diabetes Metab J. 2025. Vol. 49, № 5. P. 964–986. DOI: 10.4093/dmj.2025.0644

inability to be used for mass screening significantly limit its use in everyday practice[9]. Therefore, in recent years, increasing attention has been paid to the search for available non-invasive biomarkers that allow timely identification of patients with a high risk of developing and progressing the disease.

Of particular interest are surrogate indicators of insulin resistance, calculated on the basis of standard laboratory and anthropometric indicators. Among the integral metabolic indicators, the most studied is the triglyceride-glucose index (TyG), which is considered an indirect marker of insulin resistance. Its derivatives have also gained considerable popularity – the triglyceride-glucose -body mass index (TyG-BMI), the triglyceride-glucose index adjusted for waist circumference (TyG-WC), and the triglyceride-glucose index adjusted for waist circumference to height (TyG-WHtR), which allow simultaneously taking into account indicators of carbohydrate and lipid metabolism and characteristics of general and abdominal obesity[10], [11].

In recent years, a large amount of evidence has been accumulated that these indices allow to predict with high accuracy the development of insulin resistance, type 2 diabetes mellitus, metabolic syndrome and MASLD, and in a number of studies they surpass the traditional HOMA-IR index due to the simplicity of calculation, low cost and the possibility of wide application in clinical practice and the population[12].

1. Insulin resistance as a key link in the pathogenesis of metabolically associated steatotic liver disease

Insulin resistance (IR) is a pathological condition in which the physiological concentration of insulin is insufficient to realize its biological effects in target tissues. The most pronounced disorders develop in the liver, skeletal muscle and adipose tissue, where insulin sensitivity decreases, energy metabolism changes and lipid and glucose metabolism regulation is disrupted[13].

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[9] Kazi I. N., Kuo L., Tsai E. Noninvasive Methods for Assessing Liver Fibrosis and Steatosis. Gastroenterol Hepatol (N Y). 2024. Vol. 20, № 1. P. 21–29. PMID: 38405045.

[10] Xue Y., Xu J., Li M., Gao Y. Potential screening indicators for early diagnosis of NAFLD/MAFLD and liver fibrosis: triglyceride glucose index-related parameters. Front Endocrinol. 2022. Vol. 13. Art. 951689. DOI: 10.3389/fendo.2022.951689.

[11] Zhuang Y., Qiu L., Han D., Qiao Z., Wang F., Jiang Q., An Q., Li Y., Shangguan J., Bi X., Shen D. The association between triglyceride-glucose index and related parameters and risk of cardiovascular disease in American adults under different glucose metabolic states. Diabetol Metab Syndr. 2024. Vol. 16, № 1. Art. 102. DOI: 10.1186/s13098-024-01340-w

[12] Singh B., Saxena A. Surrogate markers of insulin resistance: A review. World J Diabetes. 2010. Vol. 1, № 2. P. 36–47. DOI: 10.4239/wjd.v1.i2.36.

[13] Yu L., Qian J., Li X. Li X, Tian M, Bai X, Yang J, Deng R, Lu C, He X, Lu A, Liu Y. Insulin resistance: mechanisms and therapeutic interventions. Mol Biomed. 2026. Vol. 7. Art. 12. DOI: 10.1186/s43556-026-00408-5.

Currently, insulin resistance is considered the main pathogenetic link of MASLD, combining obesity, type 2 diabetes, dyslipidemia and cardiovascular disease into a single continuum of metabolic dysfunction[14]. At the same time, hepatic steatosis is no longer considered solely a consequence of excessive fat consumption, but is perceived as a manifestation of systemic metabolic disorders.

Under physiological conditions, insulin inhibits lipolysis in adipocytes, stimulates glycogen synthesis, reduces hepatic glucose production, and regulates lipid metabolism. In the case of insulin resistance, these mechanisms are disrupted. Triglyceride hydrolysis in adipose tissue is enhanced, resulting in increased free fatty acid delivery to the portal vein and liver. At the same time, the stimulating effect of insulin on de novo lipogenesis is maintained, while its ability to inhibit gluconeogenesis is significantly reduced. As a result, a kind of selective hepatic insulin resistance is formed, in which lipid synthesis and hepatic glucose production are simultaneously enhanced[15]. According to modern ideas, more than 60% of lipids accumulated in the liver in MASLD are formed precisely due to the increased supply of free fatty acids from visceral adipose tissue, about 25% is due to de novo lipogenesis and only a small part comes directly with food[16], [17]. Exceeding the ability of hepatocytes to safely deposit triglycerides is accompanied by the accumulation of toxic lipid intermediates – diacylglycerols, ceramides and acylcarnitines, which have a pronounced lipotoxic effect. It should be noted that insulin resistance not only contributes to the development of MASLD, but also itself increases as the disease progresses. The accumulation of lipids in the liver is accompanied by further deterioration of insulin signal transmission, forming a kind of "vicious circle" in which steatosis and insulin resistance mutually potentiate each other. This explains the high

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[14] Colantoni A., Bucci T., Cocomello N. Angelico F, Ettorre E, Pastori D, Lip GYH, Del Ben M, Baratta F. Lipid-based insulin-resistance markers predict cardiovascular events in metabolic dysfunction associated steatotic liver disease. Cardiovasc Diabetol. 2024. Vol. 23, № 1. Art. 175. DOI: 10.1186/s12933-024-02263-6.

[15] Friedman S. L., Neuschwander-Tetri B. A., Rinella M., Sanyal A. J. Mechanisms of NAFLD development and therapeutic strategies. Nat Med. 2018. Vol. 24, № 7. P. 908–922. DOI: 10.1038/s41591-018-0104-9.

[16] Palomurto S., Virtanen K. A., Kärjä V., Schwab U., Kaminska D., Käkelä P., Pihlajamäki J., Männistö V. Metabolic Dysfunction-associated Steatotic Liver Disease Alters Fatty Acid Profiles in the Liver and Adipose Tissue. J Clin Endocrinol Metab. 2026. Vol. 111, № 1. P. e23–e31. DOI: 10.1210/clinem/dgaf346.

[17] Steinberg G. R., Valvano C. M., De Nardo W., Watt M. J. Integrative metabolism in MASLD and MASH: Pathophysiology and emerging mechanisms. J Hepatol. 2025. Vol. 83, № 2. P. 584–595. DOI: 10.1016/j.jhep.2025.02.033.

prevalence of MASLD among patients with type 2 diabetes, where the incidence of the disease, according to various studies, reaches 70–80%[18].

Given the central role of insulin resistance in the pathogenesis of MASLD, its timely assessment is of paramount clinical importance. However, direct methods for determining tissue sensitivity to insulin, primarily the hyperinsulinemic euglycemic clamp, are characterized by high cost, technical complexity and are used mainly in scientific research. Even the widely used HOMA-IR index requires determination of fasting insulin levels, which limits its use in routine clinical practice. Therefore, in recent years, more and more attention has been paid to the development of simple surrogate indicators of insulin resistance based on standard biochemical analyses. The most promising among them is the triglyceride-glucose index (TyG), and its derivative TyG-BMI is currently considered one of the most accurate non-invasive risk markers of MASLD.

In 2008, Simental-Mendía et al. first proposed the use of the triglyceride-glucose index (TyG) as a simple surrogate indicator of insulin resistance. The authors demonstrated that the index has high diagnostic accuracy in detecting insulin resistance compared with the hyperinsulinemic euglycemic clamp and can be used as an inexpensive and easily reproducible tool for mass population screening[19]. This approach is described in detail in the analyzed article, which provides the original formula for calculating TyG, shows its advantages over HOMA-IR and reviews the first studies of the diagnostic value of this index.

Later, a large number of studies were published that confirmed the high diagnostic and prognostic value of TyG in detecting type 2 diabetes, metabolic syndrome, arterial hypertension, cardiovascular diseases and MASLD. According to several large meta-analyses of recent years, the TyG index demonstrates comparable, and in some cases even higher diagnostic efficiency compared to HOMA-IR, especially in population studies where determining insulin concentration is economically impractical[20].

An important addition to international data are the results of domestic studies that evaluated the diagnostic value of TyG in patients with carbohydrate

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[18] European Association for the Study of the Liver (EASL), European Association for the Study of Diabetes (EASD), European Association for the Study of Obesity (EASO). EASL–EASD–EASO Clinical Practice Guidelines on the management of metabolic dysfunction-associated steatotic liver disease (MASLD). J Hepatol. 2024. Vol. 81, № 3. P. 492–542. DOI: 10.1016/j.jhep.2024.04.031.

[19] Simental-Mendía L. E., Rodríguez-Morán M., Guerrero-Romero F. The product of fasting glucose and triglycerides as surrogate for identifying insulin resistance in apparently healthy subjects. Metab Syndr Relat Disord. 2008. Vol. 6, № 4. P. 299–304. DOI: 10.1089/met.2008.0034

[20] Nayak S.S., Kuriyakose D., Polisetty L.D., Patil A.A., Ameen D., Bonu R., Shetty S.P., Biswas P., Ulrich M.T., Letafatkar N., Habibi A., Keivanlou M.H., Nobakht S., Alotaibi A., Hassanipour S., Amini-Salehi E. Diagnostic and prognostic value of triglyceride glucose index: a comprehensive evaluation of meta-analysis. Cardiovasc Diabetol. 2024. Vol.23, №1. P. 310. doi: 10.1186/s12933-024-02392-y.

metabolism disorders and liver pathology. Thus, Plokhotnichenko O. O., Tyzhnenko T. V. et al. in a study of patients with type 2 diabetes demonstrated significantly higher TyG values in patients with nonalcoholic fatty liver disease compared to patients without NAFLD (8.52 ± 0.68 vs. 7.95 ± 0.76; p = 0.004). Based on the results of logistic regression and ROC analysis, the authors determined a threshold value of TyG 8.018 for forming a risk group for NAFLD. In addition, a relationship between TyG and indicators of insulin resistance, lipid metabolism, oxidative stress, adipokines, and chronic inflammation parameters was established, which further confirms the pathophysiological validity of using this index to assess metabolic risk[21].

Thus, the accumulated data indicate the feasibility of using TyG as an accessible non-invasive indicator that integrates information about carbohydrate and lipid metabolism disorders and can be used for metabolic risk stratification and early detection of patients with MASLD. At the same time, given the close relationship between insulin resistance and excess body weight and obesity, further improvement of the diagnostic informativeness of TyG is associated with its combination with anthropometric indicators. One of the most promising options is TyG-BMI – a triglyceride-glucose index adjusted for body mass index, which simultaneously takes into account metabolic disorders and the degree of obesity.

2. Background to the TyG-BMI Index

Of particular interest in the context of MASLD are derivatives of the triglyceride-glucose index, which combine its metabolic component with anthropometric characteristics of obesity. Among them, the triglyceride-glucose index adjusted for body mass index (TyG-BMI), which integrates an indirect marker of insulin resistance with an indicator of overweight and obesity, attracts special attention. Data from modern studies and meta-analyses indicate a significant association of TyG-BMI with the presence of MASLD and its potential diagnostic value for identifying individuals at increased risk of the disease. Thus, given the pathophysiological relationship between insulin resistance, lipid metabolism disorders, and excess adipose tissue accumulation in MASLD, the use of the combined TyG-BMI index may be more informative than the assessment of individual metabolic or anthropometric indicators. That is why in our study, for a comprehensive assessment of metabolic risk and its relationship with MASLD, the triglyceride-glucose index adjusted for body

[21] Plohotnichenko O. O., Tyzhnenko T. V., Misyura K. V., Kravchun N. O., Gorshunska M. Yu., Pochernyaev A. K. et al. Triglyceride-glucose index as a new non-invasive criterion in the diagnosis of non-alcoholic fatty liver disease in patients with type 2 diabetes. Problems of endocrine pathology. 2025;82(1):25–32.

mass index (TyG-BMI), which is calculated as the product of the TyG index and the body mass index (BMI), will be used. Unlike the classic TyG, this index reflects not only the biochemical manifestations of insulin resistance, but also the influence of total body fat mass, which significantly increases its sensitivity in the diagnosis of MASLD, especially in patients with obesity and type 2 diabetes[22], [23].

Despite the high diagnostic value of the triglyceride-glucose index (TyG), the data accumulated to date indicate that its use has certain limitations. The main disadvantage of the classic TyG is the lack of accounting for the degree of obesity, which in itself is one of the most significant factors in the formation of insulin resistance and metabolically associated steatotic liver disease (MASLD).

Visceral adipose tissue is not only an energy depot, but also an active endocrine organ. Adipocytes secrete a wide range of biologically active substances – leptin, adiponectin, resistin, visfatin, retinol-binding protein-4, tumor necrosis factor (TNF-α), interleukin-6 and other mediators of chronic inflammation. Excessive accumulation of visceral fat is accompanied by impaired secretion of these factors, the development of low-intensity systemic inflammation, increased lipolysis and an increase in the supply of free fatty acids to the liver[24].

Therefore, it became obvious that laboratory indicators of insulin resistance should be combined with anthropometric characteristics of obesity. This approach allows you to simultaneously take into account both metabolic disorders and the degree of excessive accumulation of adipose tissue.

3. Pathophysiological justification of TyG-BMI and diagnostic potential

The modern concept of the development of MASLD is based on the multiple-hit hypothesis model, according to which the formation of the disease is due to the simultaneous action of many factors: insulin resistance, visceral obesity, chronic inflammation, oxidative stress, changes in the intestinal microbiota, genetic characteristics and disorders of adipokines secretion.

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[22] Song K., Xu Y., Wu S., Zhang X., Wang Y. Pan S. Research status of triglyceride glucose-body mass index (TyG-BMI index). Front. Cardiovasc. Med. 2025. Vol. 12:1597112. doi: 10.3389/fcvm.2025.1597112

[23] Du K, Huang Y, Yu Y, Guo J, Feng J, Jiang F. Diagnosis of metabolic dysfunction-associated steatotic liver disease by triglyceride glucose-body mass index: A systematic review and meta-analysis. Ann Hepatol. 2026.102122. doi: 10.1016/j.aohep.2025.102122.

[24] Bansal S., Vachher M., Arora T., Kumar B., Burman A., Visceral fat: A key mediator of NAFLD development and progression Human Nutrition & Metabolism, 2023, Vol. 33, 200210 https://doi.org/10.1016/j.hnm.2023.200210.

Classical TyG mainly reflects disorders of carbohydrate and lipid metabolism. However, the severity of hepatic steatosis is determined not only by the degree of insulin resistance, but also by the amount of visceral adipose tissue.

It is the increase in visceral fat mass that leads to:

- an increase in the concentration of free fatty acids in the portal circulation;
- increased hepatic lipogenesis;
- accumulation of toxic lipid intermediates;
- activation of Kupffer cells;
- stimulation of hepatic stellate cells;
- development of inflammation and fibrosis.

Thus, the inclusion of BMI allows TyG-BMI to more fully reflect the total metabolic load on the liver.

The TyG-BMI index is calculated as the product of the classical TyG index and the body mass index:

$$\text{TyG-BMI} = \text{TyG} \times \text{BMI}$$

where

- TyG is the triglyceride-glucose index;
- BMI is the body mass index (kg/m^2).

Despite the extremely simple mathematical model, TyG-BMI combines three most important components of the pathogenesis of metabolic diseases:

- carbohydrate metabolism disorders;
- lipid metabolism disorders;
- severity of obesity.

Due to this, the index reflects not only the presence of insulin resistance, but also the degree of its clinical implementation.

It should be noted that the body mass index is not an ideal indicator of obesity and does not allow assessing the distribution of adipose tissue. However, BMI remains the most accessible anthropometric characteristic, widely used both in clinical practice and in large population studies.

It is the studies of the last five years that have made TyG-BMI one of the most discussed indices in modern hepatology. Almost all large cohort studies have shown an independent association of TyG-BMI with:

- the presence of hepatic steatosis;
- the severity of fatty infiltration;
- the presence of steatohepatitis;
- the development of significant fibrosis;
- an increased risk of cirrhosis.

TyG-BMI retains a high prognostic value even in individuals with normal blood glucose levels. This indicates the possibility of using this indicator to detect early stages of metabolic disorders before their clinical manifestation.

The main advantages of TyG-BMI include:

- simplicity of calculation;
- use of only routine laboratory indicators;
- no need to determine insulin;
- low cost;
- high reproducibility;
- possibility of automatic calculation by laboratory information systems;
- high diagnostic efficiency in MASLD;
- possibility of mass screening of the population.

Most modern recommendations consider TyG-BMI as a risk stratification tool, and not an independent diagnostic criterion for MASLD[25].

Despite the rapid development of non-invasive diagnostic methods, none of the considered indices can yet replace instrumental methods of liver assessment. Their main purpose is to stratify the risk, identify patients who need a more in-depth examination (for example, elastography or MRI with determination of the liver fat fraction), as well as dynamically monitor the effectiveness of therapeutic measures.

In this regard, TyG-BMI has a number of practical advantages: the index is calculated on the basis of data that are almost always available to the primary care physician, does not require additional costs and is easily integrated into electronic medical systems. This makes it a promising tool for mass screening programs for patients with obesity, type 2 diabetes mellitus and other components of the metabolic syndrome. However, further prospective studies are needed to standardize the threshold values of TyG-BMI for different ethnic groups and clinical categories of patients.

Over the past ten years, interest in the triglyceride-glucose index has increased significantly. If initially studies were aimed exclusively at assessing the relationship between TyG and insulin resistance and type 2 diabetes mellitus, then since 2020 most publications have been devoted to studying the role of derivatives of the index, primarily TyG-BMI, in the diagnosis and prediction of MASLD[26].

It should be noted that most published studies have been performed in East Asian countries, primarily in China, South Korea, and Japan, where the prevalence of MASLD is extremely high. In recent years, the number of studies

[25] Zhu X., Wang Z., Yang X., Ning Z. Diagnostic performance of TyG-related indices for MAFLD screening in older adults at moderate altitude: TyG-BMI showed the highest discriminatory ability. BMC Gastroenterol 26, 172 (2026). https://doi.org/10.1186/s12876-026-04604-z.

[26] Chen L., Tang Y., Guo H., Jiang W., Deng X., Interpreting the triglyceride–glucose index and its derived indices in metabolic dysfunction-associated steatotic liver disease: clinical utility and evidence gaps. Front Med. 2026. Vol. 13. Art. 1857612. DOI: 10.3389/fmed.2026.1857612.

conducted in European and North American populations has been actively increasing, which contributes to the confirmation of the universal diagnostic value of TyG-BMI[27].

4. Clinical significance of TyG-BMI in patients with type 2 diabetes mellitus

The use of TyG-BMI in patients with type 2 diabetes is of particular interest, since this category is characterized by the highest prevalence of MASLD

According to current data, signs of hepatic steatosis are detected in more than two thirds of patients with diabetes, while the frequency of development of pronounced fibrosis significantly exceeds the indicators of the general population[28].

Several studies have shown that TyG-BMI is more associated with the presence of MASLD in patients with type 2 diabetes than classic TyG. Moreover, the diagnostic value of the index was maintained regardless of the duration of the disease, the level of glycated hemoglobin and the glucose-lowering therapy being carried out[29]. The obtained data allow us to consider TyG-BMI as a potential tool for the initial selection of patients who require liver elastography or other methods of in-depth diagnostics.

In addition to diagnosing an existing disease, TyG-BMI is actively studied as a predictor of the future development of MASLD.

A particularly pronounced prognostic value of the index is noted in patients with obesity, prediabetes and metabolic syndrome. In these groups, TyG-BMI allows identifying individuals at highest risk of developing the disease even before the appearance of pronounced laboratory changes in liver function.

Therefore, the index can be used not only as a diagnostic but also as a prognostic tool with the organization of preventive programs.

Despite the large number of publications, the evidence base of TyG-BMI has a number of limitations.

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[27] Boushehri Y. G., Meymanatabadi Z., Tanha A. E., Azami P., Alaei M., Alamdari A.A., Momtazi H., Moezzi N.D., Habibzadeh A., Khanmohammadi S. Association of triglyceride glucose-body mass index (TyG-BMI) with metabolic dysfunction-associated steatotic liver disease: A systematic review and meta-analysis. PLoS One. 2025. Vol. 20, № 8. Art. e0324483. DOI: 10.1371/journal.pone.0324483

[28] En Li., Cho E., Ang C.Z., Quek J., Fu C.E., Lim L.K.E., Heng Z.E.Q., Tan D.J.H., Lim W.H., Yong J.N., Zeng R., Chee D., Nah B., Lesmana C.R.A., Bwa A.H., Win K.M., Faulkner C., Aboona M.B., Lim M.C., Syn N., Kulkarni A.V., Suzuki H., Takahashi H., Tamaki N., Wijarnpreecha K., Huang D.Q., Muthiah M., Ng C.H., Loomba R. Global prevalence of non-alcoholic fatty liver disease in type 2 diabetes mellitus: an updated systematic review and meta-analysis. Gut. 2023 Vol. 11., P. 2138–2148. DOI: 10.1136/gutjnl-2023-330110

[29] He Q.J., Xu Y.Y., Tan X., Yin Y.C. Triglyceride-glucose body mass index and metabolic dysfunction-associated steatotic liver disease in hospitalized patients with type 2 diabetes: a sex-stratified cross-sectional study. BMC Endocr Disord. 2026. Vol. 26., P. 165. doi: 10.1186/s12902-026-02321-y.

A significant part of the work was carried out in Asian populations, which differ in the characteristics of the distribution of adipose tissue, eating behavior and genetic predisposition. This limits the possibility of direct extrapolation of the results obtained to the European population. Thirdly, there are no single generally accepted cut-off values of TyG-BMI. The difference between studies is due to the different criteria for diagnosing MASLD, the age composition of the samples, the prevalence of obesity and diabetes mellitus, as well as the use of different liver imaging methods.

5. Materials and methods of our own study

61 patients with type 2 diabetes were examined (34/27 men/women; age 53±1.20 years; disease duration 13.36±3.49 years; of them – with MASLD (n=24) without MASLD (n=37). The diagnosis of MASLD was established on the basis of clinical analysis of the disease, lipid and carbohydrate metabolism indicators, aminotransferase (AST) activity, alanine aminotransferase (ALT) activity and ultrasound examination of the liver. Determination of total cholesterol (TC), high-density lipoprotein cholesterol (HDL), triglycerides was performed by enzymatic method. Free fatty acids (FFA) were measured using a Wako Diagnostics kit (USA). According to the manufacturer's instructions for using enzyme-linked immunosorbent assay (ELISA), the levels of adipocytokines, such as adiponectin, leptin, progranulin and others, as well as insulin (DRG, Germany). IR was calculated using the HOMA-IR (Homeostasis Model Assessment-Insulin Resistance) index[30], which includes simultaneous determination of individual fasting serum insulin and glucose levels. Insulin sensitivity was determined using the QUICKI (Quantitative Insulin Check Index) index[31].

To assess the diagnostic properties of the TyG index, discriminant analysis was used, and the sensitivity, specificity, positive prognostic value (PPV) and negative prognostic value (NPV) of the results, and the accuracy index were calculated.

6. Results of our own study and their discussion

The studied group (except for the control group) consisted exclusively of patients with type 2 diabetes with an insulin-resistant phenotype (body

[30] Matthews, D.R. Hosker J.P., Rudenski A.S., Naylor B.A., Treacher D.F., Turner R.C. Homeostasis model assessment: insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man. Diabetologia – 1985; – Vol. 28. – P. 412–419

[31] Katz A., Nambi S.S., Mather K., Baron A.D., Follmann D.A., Sullivan G., Quon M.J.,Quantitative insulin sensitivity check index: a simple, accurate method for assessing insulin sensitivity in humans. J Clin Endocrinol Metab. – 2000. – Vol. 85(7) – P. 2402–2410

mass index (BMI): kg/m2, HOMA-IR, QUICKI, etc.) with varying degrees of glycemic control (HbA1c). The TyG index is generally an accessible and simple indicator in practical use. Patients with MASLD are characterized by a higher TyG-BMI index (295.88±56.53) than the group without MASLD (248.27±39.38; t=3.64; p=0.0006). In patients with T2DM, an increased TyG-BMI is associated with the presence of MASLD and markers of insulin resistance and metabolic dysfunction; The indicator may be a promising tool for primary metabolic stratification, but requires validation and integration into existing algorithms for non-invasive assessment of MASLD. Patients with type 2 diabetes were divided into groups to further determine the expression of hormonal and metabolic disorders depending on the state of the liver (present and absent MASLD) (Table 1).

Table 1

Anthropometric, laboratory and instrumental parameters in patients with type 2 diabetes mellitus depending on the presence of MASLD

Indicator	Control Patients	Patients with MASLD ($\overline{X} \pm s\overline{X}$)	Patients without MASLD ($\overline{X} \pm s\overline{X}$)	P
BMI, kg/m2	26,80±0,76	33,36±0,40	30,56±0,28	**<0,001**
Waist/hip ratio	0,78±0,01	1,00±0,01	0,96±0,01	**<0,01**
Glucose, mmol/l	5,21±0,11	9,91±0,24	9,51±0,34	>0,05
HbA1c, %	5,4±0,10	7,52±0,11	7,65±0,28	>0,05
Systolic BP, mmHg	123,36±5,20	150,19±3,14	143,80±2,10	**<0,1**
Diastolic BP, mmHg	79,42±3,41	89,42±1,53	83,86±1,16	**<0,001**
Insulin, pmol/l	85,21±8,00	144,28±9,67	127,69±8,65	>0,05
HOMA-IR index, ud.units	3,06±0,28	9,95±0,76	7,89±0,50	**<0,05**
QUICKI, ud.units	0,56±0,01	0,46±0,01	0,48±0,01	>0,05
HDL cholesterol, mmol/l	1,54±0,17	1,08±0,02	1,26±0,05	<0,001
LDL cholesterol, mmol/l	3,84±0,30	3,76±0,10	3,52±0,08	<0,1
Triglycerides, mmol/l	1,56±0,20	3,53±0,21	2,49±0,15	**<0,001**
FFA, mmol/l	0,70±0,06	1,37±0,05	1,33±0,04	>0,05
Adiponectin, mg/l	11,75±1,33	4,68±0,27	4,92±0,21	>0,05
Leptin, ng/ml	10,55±1,68	84,73±13,80	52,57±6,86	<0,01

Note 1. BMI – body mass index.

Note 2. HbA1c – glycosylated hemoglobin.

Note 3. BP – blood pressure.

Note 4. HOMA-IR – Homeostatic Model Assessment insulin resistance index.

Note 5. QUICKI – Quantitative Insulin Sensitivity Check Index.

Note 6. HDL – high-density lipoprotein.

Note 7. LDL – low-density lipoprotein.

Note 8. FFA – free fatty acids.

By localization, in all examined patients with type 2 diabetes mellitus complicated by MASLD, obesity is abdominal, because the waist-to-hip ratio (WHR) for these patients is 1.00±0.01. In addition, the WHR among patients with type 2 diabetes mellitus with MASLD is higher ($p<0.01$) than among patients with type 2 diabetes mellitus without MASLD. Abdominal (visceral) type of obesity is a significant risk factor for MASLD. In the examined diabetic population, an increase in the insulin resistance index HOMA-IR was verified in patients with type 2 diabetes mellitus with MASLD ($p<0.05$) compared to the group of patients with type 2 diabetes mellitus, uncomplicated MASLD. In patients with MASLD, a more pronounced atherogenic lipid phenotype is formed, i.e. an increase in triglycerides in combination with a decrease in HDL is noted. The identified changes may be pathogenetically related to the more pronounced insulin resistance characteristic of patients with MASLD. Under conditions of insulin resistance, lipolysis in adipose tissue and the influx of free fatty acids to the liver are enhanced, de novo lipogenesis is activated, and the synthesis and secretion of triglyceride-rich very low-density lipoproteins (VLDL) are increased. At the same time, the clearance of triglyceride-rich lipoproteins is impaired, which contributes to the accumulation of triglycerides in the circulation. Disturbance of HDL metabolism additionally leads to a decrease in its concentration[32] Thus, the combination of hypertriglyceridemia and low HDL levels can be considered as a metabolic reflection of systemic insulin resistance and impaired hepatic lipid homeostasis, which accompany MASLD.

Moreover, both indicators, both triglycerides and HDL, correspond to the cardiometabolic characteristics used in the current definition of MASLD. The combination of hypertriglyceridemia and low HDL levels reflects the close relationship between insulin resistance, impaired lipid metabolism and fat accumulation in the liver, which justifies the feasibility of using integral

[32] Soto A., Spongberg C., Martinino A., Giovinazzo F. Exploring the Multifaceted Landscape of MASLD: A Comprehensive Synthesis of Recent Studies, from Pathophysiology to Organoids and Beyond. Biomedicines. 2024. Vol. 12, № 2. Art. 397. DOI: 10.3390/biomedicines12020397.

Table 2

Characteristics of correlations of the index TyG-BMI index

Indicator	Spearman – R	P
TYG-BMI & Glycated hemoglobin (HbA1c), %	-0,002	0,98
TYG-BMI & Insulin, pmol/l	0,33	0,01
TYG-BMI & HOMA-IR, ud.units	0,37	0,006
TYG-BMI & QUICKI, ud.units	-0,37	0,006
TYG-BMI & AST IU/L	0,20	0,17
TYG-BMI & ALT IU/L	0,06	0,66
TYG-BMI & FFA, mmol/ml	0,21	0,12
TYG-BMI & Adiponectin, μg/ml	0,23	0,20
TYG-BMI & HMW, μg/ml	0,26	0,14
TYG-BMI & Prothrombin Index, %	0,35	0,01
TYG-BMI & Fibrinogen, g/l	-0,05	0,70
TYG-BMI & Fibrin, mg	-0,05	0,70
TYG-BMI & Fibrinolytic Activity, min.	-0,26	0,09
TYG-BMI & Blood Urea, mmol/l	0,24	0,08
TYG-BMI & Leptin ng/ml	0,46	0,007
TYG-BMI & C-Reactive Protein pg/mol	0,33	0,01
TYG-BMI & Osteoprotegerin, pg/ml	0,28	0,12

metabolic indices, in particular TyG and TyG-BMI, to assess the risk of MASLD.

Note 1. HOMA-IR – Homeostatic Model Assessment insulin resistance index.

Note 2. QUICKI – Quantitative Insulin Sensitivity Check Index

Note 3. AST – Aspartate Aminotransferase

Note 4. ALT – Alanine Aminotransferase

Note 5. FFA – free fatty acids.

Note 6. HDL – high-density lipoprotein.

Note 7 HMW –High-molecular weight adiponectin

Note 8. Spearman R – Spearman's rank correlation coefficient

TyG-BMI is associated not only with the presence of hepatic steatosis but also with the metabolic phenotype underlying MASLD, including insulin resistance and adipose-tissue dysfunction.

The identified correlations are consistent with the pathophysiological concept of the relationship between TyG-BMI and insulin resistance, adipose tissue dysfunction and systemic inflammation. A significant positive correlation

between TyG-BMI and: insulin (r=0.327; p=0.01) and HOMA-IR (r=0.367; p=0.0068) was identified. That is, with an increase in TyG-BMI, the severity of insulin resistance increases. TyG-BMI combines the triglyceride-glucose component, which reflects metabolic insulin resistance, with BMI, which characterizes excess fat mass. Therefore, this index potentially reflects two interconnected components of metabolic dysfunction at once. Insulin resistance is one of the central mechanisms of MASLD: it promotes increased lipolysis, fatty acid entry into the liver, and maintenance of stimulated lipogenesis even in the presence of impaired insulin regulation[33]. The positive relationship of TyG-BMI with HOMA-IR and the negative relationship with QUICKI indicate the consistency of TyG-BMI with two independent surrogate characteristics of insulin resistance/insulin sensitivity.

TyG-BMI was positively correlated with leptin levels (r=0.46; p=0.007), which may reflect the relationship between excess adipose tissue, insulin resistance, and adipokine dysregulation. An increase in adipose tissue mass is accompanied by increased leptin production, while in obesity its increased concentration is often combined with a decrease in leptin sensitivity (leptin resistance). The obtained correlation indicates a close relationship between the integral metabolic dysfunction reflected by TyG-BMI and adipose tissue dysfunction, which is one of the pathogenetic components of the development of MASLD. The associations of TyG-BMI with HOMA-IR and QUICKI provide internal biological consistency of the observed relationship, as higher TyG-BMI was associated with greater insulin resistance and lower insulin sensitivity.

The task was set to identify, evaluate from a pathophysiological point of view and calculate mathematically the properties, primarily the relevance of the TyG-BMI index, as a new non-invasive indicator for diagnosing MASLD in the diabetic population. To assess the relevance, the method was used Discriminant analysis is one of the types of multivariate statistics that allows studying the differences between individual groups of objects by several characteristics simultaneously. The purpose of discriminant analysis is to classify an object, i.e. to attribute it to one of several predetermined groups – classes, based on the measurement of various characteristics (characteristics, parameters). The characteristics according to which the object is classified are called discriminant variables. The discriminant variables should be on an interval or ratio scale and be independent (i.e., variables included in the same model should not be highly

[33] Bo T., Gao L., Yao Z., Shao S., Wang X., Proud C.G., Zhao J. Hepatic selective insulin resistance at the intersection of insulin signaling and metabolic dysfunction-associated steatotic liver disease. Cell Metab. 2024;Vol36., P. 947-968. doi:10.1016/j.cmet.2024.04.006.

correlated with each other with a correlation coefficient approaching 1). It is desirable that the distribution of each of the variables corresponds to normal.

Based on preliminary calculations, these indicators were used to build a mathematical model using discriminant analysis. A complete data set was available for discriminant analysis in 54 patients; 7 patients were excluded from the classification analysis due to the absence of individual parameters.

At the first stage of the analysis, the informativeness and statistical significance of the differences in the features in the studied groups were assessed. The procedures of discriminant analysis are represented by interpretation methods and classification methods. Using interpretation methods, the selection of characteristics (variables, features) is carried out, which allow to distinguish one class (group) from another, determine how well these characteristics allow to make a distinction, and which of them are the most informative. The method related to classification is associated with obtaining one or more functions that provide the ability to attribute a given object to one of the groups (for example, healthy/sick, there is a risk of developing a disease, or there is no risk). The practical task of discriminant analysis is to attribute an object to one of the existing classes (groups). Discriminant analysis is used in various fields, in medicine, for example, it is used to assess the probability of developing (or having) a disease, and to form risk groups. Classes are formed on the basis of a classifying variable, which is presented in a scale of names (for example, healthy/sick). The assignment of an object to a particular class is based on the discriminant function. The number, significance of discriminant functions and their values are determined to explain the differences between classes (when there are 2 classes, one discriminant function is calculated). By means of discriminant analysis, such values of coefficients are found, with which objects can be divided into groups as accurately as possible.

Different types of multivariate statistics have common basic principles, therefore the discriminant function is similar to the logistic regression function:

The basic discriminant function has the following form:

$$d_{km} = \beta_0 + \beta_1 x_{1km} + \ldots + \beta_p x_{pkm}, \quad m = 1,\ldots,n, \;\; k = 1,\ldots,g$$

where d_{km} – the value of the discriminant function for the m-th object in group k; the value of the discriminant variable for the m-th object in group *k,* x – the values of the variables corresponding to the given cases (the values of the studied indicators in specific patients), β_0, β_1 – the coefficients that will be determined using discriminant analysis.

A feature of discriminant analysis is the presence of a special sample – a group that includes objects with a known class affiliation. This sample is used to perform calculations and identify patterns, and to construct the corresponding

equations that will later allow determining which class new objects belong to. Using discriminant analysis, objects can be divided into a larger number of groups. Then, when conducting discriminant analysis, several discriminant functions are derived.

Statistically significant ones are selected from them. Discriminant functions can have different predictive qualities (reliability), so the division into groups occurs with varying success. It is easier to distinguish a group that differs from others more strongly than others, and it is more difficult to divide groups that differ less. The criterion for the correctness of division into groups is the Wilks λ statistic, with which the level of significance is established. If the level of significance reaches a critical level ($p \leq 0.05$), it can be assumed that the use of the specified features can be reliably used for classification using the discriminant function. In order to exclude multicollinearity in discriminant analysis, an indicator such as tolerance (To) is calculated, it reflects the degree of lack of correlation of the feature with all others, this is the magnitude of the variability of the feature, which cannot be estimated by other features. If the tolerance of a feature is close to zero, then it is better to exclude it from further analysis as uninformative, that is, the greater the value of tolerance, the more important (informative) this feature is for classification (in medicine – for diagnosis)[34], [35].

Conducting discriminant analysis includes several stages:

1) selection of features for constructing a classification function

2) construction of a classification function

3) assessment of the quality of the function

The assessment of the informativeness of the feature is carried out using the Wilks criterion and the tolerance value (To), in turn, the determination of the statistical significance of the Wilks statistic is carried out using the Fisher criterion.

At the first stage, the selection of features is carried out using the indicators: λ Wilks, partial λ Wilks, Fisher criterion, and tolerance.

λ Wilks

The λ Wilks statistic is calculated as the ratio of the determinant of the intragroup variance matrix to the determinant of the general covariance matrix.

According to the formula: $\lambda = \det(W)/\det(T)$

where T is the intergroup and W is the intragroup dispersion matrix of variables from the means.

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[34] Lachenbruch P. A. Discriminant Analysis. In: Wiley StatsRef: Statistics Reference Online / eds. N. Balakrishnan, T. Colton, B. Everitt, W. Piegorsch, F. Ruggeri, J. L. Teugels. 2014. DOI: 10.1002/9781118445112.stat02434

[35] Backhaus K., Erichson B., Gensler S., et al. Multivariate analysis: an application-oriented introduction. Cham: Springer, 2021. 607 p. DOI: 10.1007/978-3-658-32589-3.

The elements of the matrix T are determined by the ratio:

$$t_{ij} = \sum_{k=1}^{g} \sum_{m=1}^{n} (x_{ikm} - \bar{x}_i)(x_{jkm} - \bar{x}_j)$$

Matrix W – ratio – $w_{ij} = \sum_{k=1}^{g} \sum_{m=1}^{n_k} (x_{ikm} - \bar{x}_{ik})(x_{jkm} - \bar{x}_{jk})$

Where:

g – number of groups;

p – number of discriminant variables;

nk – number of observations in the k-th group;

n – total number of observations in all groups;

X_{ikm} – value of variable i for the m-th observation in the k-th group;

$X_{ik.}$ – average value of variable i in the k-th class;

$X_{i.}$ – average value of variable i across all groups (general average).

Matrix W, differs from T in that its elements are determined by the average values of variables for individual groups, and not by general averages.

Partial λ Wilks – λp (Partial Lambda). This is the λ Wilks statistic, which characterizes the contribution of a separate corresponding variable to the discrimination between groups. It is calculated as the ratio of λ Wilks after adding the corresponding variable to λ Wilks before adding this variable.

$$\text{partial } \lambda = \lambda(\text{after}) / \lambda(\text{before})$$

This value can be considered as an analogue of the partial correlation coefficient. It should be noted that the smaller the partial λ, the greater the contribution to the overall discrimination.

The Fisher test (F) is also used to determine the level of statistical significance of the indicators λ and λp.

$F=S_1^2/S_2^2$, where S_1^2 is the intergroup variance of the trait, and S_2^2 is the intragroup variance of the trait, the model includes those traits for which the significance level $p<0.05$, the greater S_1^2 and the less S_2^2, i.e. the greater the corresponding F value, the greater the classification informativeness of the trait.

In discriminant analysis, Fisher's exact test is usually calculated as follows:

$$F = [(n-q-p)/(q-1)]*[(1- \lambda p)/ \lambda p]$$

where:

n – number of observations

q – number of groups

p – number of variables

Tolerance (To) is defined as 1-R2, where R is the multiple correlation coefficient of the specified variable with all other variables included in the given

model. In turn, the multiple correlation coefficient is calculated by the formula:

$$r_{x(yz)}=\sqrt{\frac{r_{xy}^2+r_{xz}^2-2r_{xy}r_{xz}r_{yz}}{1-r_{yz}^2}}$$

2) Classification Functions

Classification is the process by which a decision is made: a given object "belongs to" or "is very similar to" a given group (class). Such a decision is made on the basis of information contained in the discriminant variables.

The classification function has the following general form:

$h_k=b_{k0}+b_{k1}X_1+b_{k2}X_2+\ldots+b_{kp}X_p$

where h_k – function value for class k, a b_{k1} – coefficients that need to be calculated, each class corresponds to its own function.

The object belongs to the class with the largest value (the largest h). The coefficients for the classification functions are determined using the following calculations:

$$b_{ki}=(n-g)\sum_{j=1}^{p}(w^{-1})_{ij}\,\overline{x}_{jk},\ \ k=1,\ldots,g$$

де b_{k1} – coefficient for variable i in the expression corresponding to the class k, a

$(w^{-1})_{ij}$ – the inverse element of the intragroup matrix of sums of pairwise multiplications W.

The constant is defined as follows:

$$b_{k0}=-0,5\cdot\sum_{j=1}^{p}b_{kj}\overline{x}_{jk},\ \ k=1,\ldots,g$$

The exact values of the function do not play a significant role: you only need to know for which class this value is the largest.

3) Before applying the results of the analysis for practical use, it is first necessary to determine the level of statistical significance of the discriminant function, for this purpose a modification of the Wilks statistic Λ (lambda) is also used, which determines how much the average values of the discriminant function in the studied groups differ, and whether this difference is significant (i.e. whether it can be used to classify, determine the presence of a disease, or complications). The level of statistical significance Λ is determined using the χ^2 criterion, if χ^2 reaches a critical level, the function can be considered

statistically significant (i.e. suitable for use). Although there are several ways to calculate it, we will use the following formula:

$$\Lambda = \prod_{i=k+1}^{g} (1/(1+\lambda_i))$$

where k – the number of functions already calculated, and the symbol P means that to obtain the final result it is necessary to multiply all variables, and λi is the eigenvalue of the function.

The statistical significance of the function is checked using the Wilks statistic Λ and the criterion χ^2:

$$\chi^2 = -[n-((p+g)/2)-1]\ln\Lambda_k, \quad k = 0,1,\ldots,g-1$$

Another characteristic that allows us to assess the quality of the discriminant function is the canonical correlation coefficient ri. The canonical correlation is a measure of the relationship between two sets of variables. The maximum value of this coefficient is 1. We will assume that the groups make up one set, and the other set is formed by the discriminant variables (i.e., it reflects the dependence between the groups and the discriminant function). The canonical correlation coefficient for the i-th discriminant function is determined by the formula:

$$r_i = \sqrt{\frac{\lambda_i}{1+\lambda_i}}.$$

where i – number of the corresponding discriminant function.

The larger the value of r_i, the better the resolution of the discriminant function.

The most important criterion for the correctness of the constructed classifier is practice, therefore, in addition to the indicators used directly when conducting discriminant analysis, for practical application of the model it is advisable to calculate additional diagnostic characteristics that show its quality. For this purpose, a classification table is used.

When conducting the analysis, the categorical indicator "MASLD development" was adopted as a grouping variable, which has two possible values "yes"/"no".

At the initial stage of the analysis, the informativeness and statistical significance of the differences in the features in the studied groups were assessed.

The criteria λ, λp, and F indicate that only one of the predictors included in the model is statistically significant, and it will be used in practice in the future,

Table 3

Discriminant analysis results (general)

Indicator	Λ	Λp	F	To	P
TYG-BMI	0,84	0,69	9,75	0,71	**0,004**
Fetuin,ug/ml	0,58	0,99	0,10	0,62	0,74
Lipocalin, ng/ml	0,59	0,98	0,35	0,70	0,55
Vaspin,ng/ml	0,58	0,99	0,02	0,76	0,86
Leptine, ng/ml	0,59	0,99	0,17	0,70	0,68
Progranulin, ng/ml	0,59	0,98	0,32	0,62	0,57
Resistin, ng/ml	0,58	0,99	0,06	0,70	0,80
Omentin-1, ng/ml	0,58	0,99	0,006	0,61	0,93
Tumor Necrosis Factor alpha, ng/ml	0,59	0,97	0,48	0,79	0,49

which requires further adjustment of the calculations. Tolerance indicators (To) indicate the absence of multicollinearity (i.e., the features do not have a significant effect on each other).

Table 4

Results of discriminant analysis (final for a statistically significant predictor)

Indicator	λ	Λp	F	To	p
TYG-BMI	1,00	0,79	13,32	1,000000	0,0006

Note: λ is the Wilks statistic, λp is Wilks' partial λ, Fisher's F test, To tolerance, p is the level of significance.

The selected method has a number of advantages, namely, it takes into account the variability of the features and considers their totality, during which coefficients are determined that reflect the specific weight of TYG-BMI in the formation of MASLD, that is, the diagnostic informativeness of a particular feature is actually established. Analysis of the contribution of the selected variables to the classification, first of all, demonstrates the high significance of the cumulative discriminant ability (F = 13.32; p = 0.0006). The criteria λ, λp, and F indicate the statistical significance of the key predictor that will be used in the model. During the discriminant analysis, equations were obtained for calculating the risk of developing MASLD.

Formulas:

1) fm = 0.13 (TyG-BMI Index) – 20.33

2) fn = 0.11 (TyG-BMI Index) – 14.27

where fm (manifestation) and fn (no manifestation) are the values of the discriminant function; 20.33 and 14.27 are constants;

The coefficients of linear discriminant functions were calculated for each of the values of the dependent characteristic in each of the two samples; results given in Table 5.

Table 5

Coefficients of classification functions obtained during discriminant analysis

Classification Functions		
	Presence of MASLD – p=0.43	Absence of MASLD – p=0.57
TYG-BMI	0,13	0,11
Constant	-20,33	-14,27

The coefficients of the classification functions of linear discriminant functions obtained during discriminant analysis are used to construct the corresponding equations, according to these equations, the function values are directly calculated, and the corresponding risk assessment for a particular patient is made.

To use the equation, should: 1) measure the corresponding indicators (X); 2) substitute the values into the equation and calculate fm and *fn*; where fm, and *fn* are the values of the discriminant function *fm* – corresponds to the presence of a complication, and *fn* – its absence. Comparing fm and fn, the patient should be classified into the group with a higher function value, i.e. if *fm* > *fn* the patient is at risk for developing MASLD

Examples:

For example, in patient N. the studied sign is:

TyG-BMI = 394.27, we substitute into the equation:

1) *fm* = 0.13 × 394.27 – 20.33 = 30.93

2) *fn* = 0.11 × 394.27 – 14.27 = 29.09

Since 30.93>29.09, i.e. *fm*>*fn*, the patient should be classified into the risk group for liver disease.

The following example:

For example, in patient K. the studied characteristic is:

TyG-BMI = 227.11, we substitute into the equation:

1) *fm* = 0.13 × 227.11 – 20.33 = 9.19

2) *fn* = 0.11 × 227.11 – 14.27 =10.71

Since 10.71>9.19, i.e. *fm*>*fn,* there is no risk for this patient.

The results of classification by TyG-BMI and the proportion of correctly classified cases are presented in the table 6.

Table 6

Classification accuracy of the TyG-BMI index in differentiating patients with and without MASLD

Classification matrix			
TYG-BMI	**Number of correct results (%)**	**With MASLD**	**Whithout MASLD**
With MASLD	39,13	9	14
Whithout MASLD	87,09	4	27
Total	66,67	13	41

Note: Matrix rows are clinically established classes, columns are predicted classes.

The diagnostic model built on the basis of TyG and BMI (TyG-BMI) demonstrated satisfactory overall diagnostic performance in risk stratification of MASLD in patients with type 2 diabetes. The sensitivity of the model was 39.13%, specificity was 87.09%, positive predictive value was 69%, negative predictive value was 65%, and overall classification accuracy was 66.67%. Of particular note is the high specificity of the model, which indicates its sufficient ability to correctly identify patients without MASLD and a limited number of false positives.

The model obtained by discriminant analysis, integrating TyG and BMI, is characterized by a balanced combination of diagnostic performance indicators and can be considered as a promising non-invasive tool for the initial metabolic stratification of patients with type 2 diabetes with respect to the risk of MASLD. Its use may be appropriate at the stage of initial selection of patients who require further in-depth examination of the liver condition.

The triglyceride–glucose–body mass index may be considered as one of the most promising non-invasive markers of metabolic dysfunction and insulin resistance. Its simplicity, low cost, excellent reproducibility, and strong biological rationale make it particularly attractive for large-scale clinical screening. Current evidence indicates that TyG-BMI consistently outperforms several traditional markers of insulin resistance for identifying individuals at increased risk of metabolic dysfunction-associated steatotic liver disease, especially among patients with obesity and type 2 diabetes mellitus. Nevertheless, TyG-BMI should be regarded as a risk assessment tool rather than a stand-alone diagnostic test. The greatest clinical benefit is likely to be achieved when TyG-BMI is incorporated into comprehensive diagnostic algorithms that combine biochemical, anthropometric, imaging, and genetic information. Future multicenter prospective studies, together with advances in artificial intelligence, precision medicine, and digital health technologies,

are expected to further define the role of TyG-BMI in the early diagnosis, prevention, and long-term management of MASLD.

CONCLUSIONS

A significant and statistically significant relationship was established between the triglyceride-glucose BMI index and the presence of liver disease.

Patients with MASLD had significantly higher TyG-BMI values than patients with T2DM without MASLD (295.88 ± 56.53 vs. 248.27 ± 39.38; $p = 0.0006$).

A distinct and significant pathogenetically substantiated correlation was established between the triglyceride-glucose BMI index and as some indicators. TyG-BMI demonstrated significant positive correlations with insulin ($r = 0.327$; $p = 0.01$), HOMA-IR ($r = 0.367$; $p = 0.0068$), leptin ($r = 0.46$; $p = 0.007$), and C-reactive protein ($r = 0.33$; $p = 0.014$), while showing an inverse correlation with QUICKI ($r = -0.367$; $p = 0.0068$). These associations support the pathophysiological relationship of TyG-BMI with insulin resistance, adipose-tissue dysfunction and low-grade systemic inflammation.

A discriminant diagnostic model was developed for the differentiation of patients with type 2 diabetes mellitus by the presence of MASLD based on the TyG index and BMI.

The proposed diagnostic model, based on the use of a new indirect non-invasive marker of insulin resistance, may be useful for developing an optimal examination algorithm and a set of measures aimed at preventing the progression of MASLD in patients with type 2 diabetes mellitus.

The obtained results support the potential use of TyG-BMI as an accessible, non-invasive and low-cost component of a stepwise MASLD risk-assessment strategy in patients with type 2 diabetes mellitus; however, its clinical applicability requires validation in larger, prospective and ethnically diverse cohorts and integration with established non-invasive liver assessment methods.

SUMMARY

The aim of the study was to determine the presence and nature of the relationship of a new indirect index of insulin resistance with the presence (or absence) of non-alcoholic fatty liver disease in patients with type 2 diabetes, as well as to determine the contribution of the TyG-BMI index to the risk of developing non-alcoholic fatty liver disease. The studied group (except for the control group) consisted exclusively of patients with type 2 diabetes with an insulin-resistant phenotype with varying degrees of glycemic control. Patients with MASLD are characterized by a higher TyG-BMI index than the group without MASLD. A significant correlation was found between the TyG index and a number of biochemical parameters: indicators of insulin resistance, adipokines,

and parameters of chronic inflammation, which clearly confirms the relationship between the TyG index and the pathogenesis of MASLD.The diagnostic model to form risk groups for non-alcoholic fatty liver disease among patients with type 2 diabetes using discriminant analysis was developed. The diagnostic criterion is a novel indicator – triglyceride-glucose index-body mass index.

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