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The Silent Pandemic: From Metabolic Consequences to Exercise and Lifestyle-Driven Remodelling in Metabolic Syndrome

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Abstract

Background: Metabolic syndrome (MetS) has emerged as one of the most critical global public health challenges of the 21st century, doubling the risk of cardiovascular events and significantly increasing all-cause mortality. Moreover, epidemiological data reflect a sharp, alarming upward trajectory in its prevalence.

Pathophysiology: This review explores the synergistic pathophysiological network of MetS. Visceral adiposity acts as the primary cellular engine, driving systemic insulin resistance. In turn, these core abnormalities trigger a cascade of downstream components, including atherogenic dyslipidaemia (the "lipid triad"), neuroendocrine-driven arterial hypertension, and systemic pro-inflammatory and pro-thrombotic states.

Diagnosis: We outline the evolution of diagnostic criteria. The consensus relies on abdominal obesity or elevated BMI as a basic criterion, combined with at least two additional factors (dysglycaemia, elevated non-HDL cholesterol, and high blood pressure).

Therapeutic Strategies: Non-pharmacological lifestyle modification — specifically the Mediterranean and DASH diets, structured aerobic and resistance training, and proper sleep hygiene — remains the absolute cornerstone of management. When lifestyle modifications fall short, modern pharmacotherapy, particularly GLP-1 receptor agonists and SGLT2 inhibitors, offers profound, synergistic cardio- and reno-protective benefits.

Conclusions: Halting the progressive multi-organ damage of metabolic syndrome requires early, holistic clinical intervention. The combination of targeted behavioural strategies and novel, organ-protective pharmacotherapies provides a powerful approach to reversing the metabolic cascade and reducing cardiovascular risk.

Key words: metabolic syndrome, visceral adiposity, insulin resistance, atherogenic dyslipidaemia, arterial hypertension, lifestyle modification.

1. Introduction

1.1. Definition and Global Burden

Metabolic syndrome (MetS) is not a single disease, but rather a complex clustering of co-occurring clinical and metabolic risk factors. Characterized by a state of chronic, low-grade systemic inflammation, MetS has emerged as one of the most critical public health challenges of the 21st century. It acts as a major driver for the development of cardiovascular diseases (CVD) and type 2 diabetes mellitus (T2DM), effectively doubling the risk of cardiovascular events and increasing all-cause mortality [1].

This growing health crisis is clearly reflected in epidemiological data from Central Europe. Recent cohort studies conducted in the Polish population demonstrate a worrisome, upward trend in the prevalence of the syndrome over the last few decades. According to the landmark WOBASZ II multi-centre national health survey (2013–2014), the overall prevalence of MetS in Poland reached 32.8% in women and 39.0% in men [2].

Furthermore, a comparative analysis spanning the decade between the original WOBASZ (2003–2005) and WOBASZ II studies reveals a sharp trajectory of growth among Polish adults aged 20 to 74 years. During this ten-year interval, the prevalence of MetS increased significantly by 3.3 percentage points in women (rising from 26.6% to 29.9%) and by a striking 8.8 percentage points in men (climbing from 30.7% to 39.4%). These findings underscore the escalating burden of metabolic disorders and highlight the urgent need for targeted public health interventions [3].

This alarming trajectory is by no means isolated to Central Europe, but rather reflects a deeply concerning global phenomenon. Most notably, data from the United States further illustrate the long-term escalation of this epidemic. According to the Centres for Disease Control and Prevention (CDC) [4], the United States witnessed a substantial 35% increase in MetS prevalence from the time the clinical term was first popularized in the 1980s up until 2012.

Taken together, these transnational trends underscore that metabolic syndrome has evolved into a truly global pandemic, transcending geographical borders and posing an ever-growing threat to healthcare systems worldwide.

1.2. Pathophysiological Underpinnings and Core Components

Metabolic syndrome arises from a sophisticated web of dysfunctional pathways, where various physiological abnormalities actively reinforce one another to accelerate the clinical course of

the syndrome. Rather than presenting as isolated clinical findings, its core components act synergistically to drive cardiovascular and metabolic deterioration [5].

At the forefront of this pathological cluster is central (visceral) adiposity, which serves as a major catalyst for the other abnormalities [6]. This ectopic fat accumulation is tightly linked to glucose intolerance and systemic insulin resistance, impairing glucose uptake in peripheral tissues and promoting hepatic gluconeogenesis [7].

Parallelly, patients exhibit a distinct atherogenic dyslipidaemia, characterized by elevated fasting triglycerides, a preponderance of small dense low-density lipoprotein (sdLDL) particles, and reduced high-density lipoprotein cholesterol (HDL-C) levels. This lipid triad, combined with arterial hypertension — driven by sympathetic nervous system overactivity and arterial stiffness — further accelerates vascular damage [8]. Crucially, this metabolic dysfunction is overlaid by chronic, systemic pro-inflammatory and pro-thrombotic states [9].

2. A Deep Dive into the Components of Metabolic Syndrome

2.1. Visceral Adiposity: The Cellular Engine of Metabolic Dysfunction

Although adipose tissue is widely distributed throughout the human body—occupying distinct anatomical niches such as subcutaneous depots, the facial region, mammary glands, bone marrow, and even investing vital organs like the heart [10] — not all fat depots carry the same pathological weight. Among these, mesenteric adipose tissue represents the most critical clinical concern in the pathogenesis of metabolic syndrome [11].

Although visceral adipose tissue constitutes only a minority of total body fat in both men and women [12], it is structurally and functionally distinct from subcutaneous depots; specifically, mesenteric fat possesses a unique anatomical advantage that translates into a major metabolic disadvantage: its venous drainage flows directly into the portal system [13]. Due to this direct vascular connection, pro-inflammatory mediators and adipokines released from mesenteric fat bypass systemic dilution in the general circulation. Instead, they hit the liver in a highly concentrated stream, making it exceptionally vulnerable to the development of hepatic insulin resistance and subsequent glucose intolerance [14].

However, it is crucial to recognize that visceral adiposity is not the sole driver of this metabolic disruption. While it acts as a primary catalyst, glucose intolerance in metabolic syndrome is inherently multifactorial [15], arising from a complex interplay of genetic predispositions, lifestyle factors, sedentary time, and neurological mechanisms that collectively impair systemic glucose homeostasis [16].

2.2. Insulin Resistance: The Core Metabolic Block

Glucose intolerance and insulin resistance represent a state in which peripheral insulin receptors become progressively desensitized — or effectively accustomed — to chronically elevated levels of circulating insulin. This phenomenon serves as a prevalent medical condition tightly linked to a spectrum of metabolic disorders, including type 2 diabetes mellitus, metabolic syndrome, hypertension, obesity, and polycystic ovary syndrome (PCOS) [17].

Under physiological conditions, insulin binding to its cell-surface receptor triggers a precise intracellular signalling cascade, allowing glucose entry into the cell. However, sustained hyperinsulinemia induces a molecular negative feedback loop. This chronic overexposure activates an array of counter-regulatory mechanisms, most notably driving the hyperactivation of specific phosphatases and negative modulators. Crucially, this state of metabolic overload converges on the activation of several intracellular kinases. Triggered by upstream cellular perturbations such as lipotoxicity, chronic inflammation, hyperglycaemia, mitochondrial dysfunction, and endoplasmic reticulum stress, these activated kinases mediate the inhibitory phosphorylation of the insulin receptor itself and its key scaffolding substrates. Consequently, this intricate network of negative feedback loops severely compromises the tissue's capacity for insulin-stimulated glucose uptake and glycogen synthesis, transforming a physiological adaptive system into a hallmark state of metabolic insulin resistance [18].

This sustained compensatory effort eventually leads to a state that temporarily maintains normal blood glucose levels, while covertly driving systemic vascular and metabolic damage long before hyperglycaemia is detected [19].

2.3. Atherogenic Dyslipidaemia: The Lipid Triad

Atherogenic dyslipidaemia is defined as a distinct metabolic abnormality characterized by the simultaneous elevation of serum triglycerides and low-density lipoprotein cholesterol, characteristically accompanied by reduced levels of high-density lipoprotein cholesterol [20]. It is widely recognized as the "lipid triad" or "atherogenic phenotype" [21].

This specific cluster of lipid derangements does not merely represent a quantitative alteration in lipid parameters, but rather a profound qualitative shift toward highly atherogenic, small dense LDL (sdLDL) particles that exponentially drive macrovascular complications [22]. The clinical significance lies in its profound capacity to accelerate the cascade of atherosclerotic cardiovascular disease [23]. Under conditions of persistent insulin resistance, the continuous influx of free fatty acids to the liver drives the overproduction of large, triglyceride-rich very-

low-density lipoprotein (VLDL) particles. This lipid overload initiates an intravascular remodelling process [24].

From a vascular standpoint, sdLDL particles possess distinct physical properties that exponentially augment cardiovascular risk. Due to their reduced size, they easily penetrate the fenestrated endothelial barrier of the arterial wall and accumulate in the subendothelial space [25]. Concurrently, the reduction in functional HDL particles impairs reverse cholesterol transport, leaving the arterial wall defenceless against progressive lipid deposition and plaque destabilization, which ultimately precipitates acute coronary syndromes and ischemic events [26].

2.4. Arterial Hypertension: Sympathetic Overactivity and Vascular Stiffness

Arterial hypertension within the metabolic syndrome is not merely a hemodynamic consequence of volume overload, but rather a complex, neuroendocrine-driven disorder. The primary driver linking metabolic dysfunction to elevated blood pressure is persistent hyperinsulinemia. Under physiological conditions, insulin acts as a weak vasodilator; however, in the state of selective insulin resistance, its metabolic signalling pathway is impaired, while its sympathetic-stimulating effects remain fully intact. Consequently, chronic hyperinsulinemia continuously stimulates the sympathetic nervous system (SNS), leading to increased cardiac output, elevated renal sodium reabsorption, and systemic vasoconstriction [27]. This sympathetic overactivity is further amplified by leptin—which is elevated due to visceral adiposity — acting directly on the hypothalamus to drive pressor responses [28].

Simultaneously, the chronic low-grade inflammatory environment and localized oxidative stress compromise vascular endothelial function [29]. The bioavailability of nitric oxide (NO) — the primary endogenous vasodilator — is drastically reduced, while the production of potent vasoconstrictors like endothelin-1 is increased [30]. This endothelial dysfunction, coupled with the proliferation of vascular smooth muscle cells stimulated by insulin and insulin-like growth factor-1 (IGF-1), initiates advanced structural remodelling of the arterial wall [8]. Over time, the elastic fibres of the media are replaced by rigid collagen, leading to progressive vascular stiffness [31]. This loss of arterial compliance increases pulse wave velocity, elevates systolic blood pressure, and accelerates microvascular damage across vital organs, establishing a vicious cycle of self-perpetuating hypertension and cardiovascular risk [32].

2.5. The Pro-inflammatory and Pro-thrombotic Cascade

The metabolic syndrome is fundamentally characterized by a chronic, sterile, low-grade systemic inflammatory state coupled with a severe prothrombotic diathesis [9]. This dual cascade is primarily orchestrated by dysfunctional visceral adipose tissue, which ceases to function merely as an energy storage depot and instead transitions into a hyperactive endocrine organ [33]. Under the influence of progressive hypertrophy and localized hypoxia, adipocytes and infiltrated immune cells drastically alter their secretory profile. This phenotypic shift results in the overproduction of classic pro-inflammatory cytokines [34], alongside a concurrent reduction in the secretion of adiponectin, a crucial cardioprotective and anti-inflammatory adipokine [35]. This persistent inflammatory milieu directly feeds into and amplifies the pro-thrombotic cascade [9]. Altogether, hepatocytes are stimulated to synthesize and secrete acute-phase reactants, most notably C-reactive protein (CRP) and fibrinogen, in response to this coordinated cascade of pro-inflammatory cytokines [36].

Simultaneously, dysfunctional visceral adipocytes markedly upregulate the expression and secretion of plasminogen activator inhibitor-1 [37]. High circulating levels of PAI-1 suppress the conversion of plasminogen to plasmin, thereby severely impairing the degradation of fibrin clots. Concurrently, systemic endothelial dysfunction, induced by chronic low-grade inflammation, promotes platelet hyperreactivity [38]. Together, this suppressed fibrinolytic capacity and enhanced procoagulant drive create a highly vulnerable systemic environment, predisposing the patient to microvascular thrombosis, accelerated atherogenesis, and catastrophic acute thrombotic occlusions during plaque rupture.

3. Diagnostics of Metabolic Syndrome

The clinical diagnosis of metabolic syndrome has historically been a subject of significant debate among major global health organizations, including the World Health Organization (WHO), the European Group for the Study of Insulin Resistance (EGIR), and the National Cholesterol Education Program (NCEP). Early diagnostic models differed substantially, with some prioritizing insulin resistance as an obligatory criterion, while others focused primarily on the manifestation of cardiovascular risk factors without requiring direct proof of insulin dysfunction. To resolve these discrepancies and establish a unified clinical approach, a joint interim statement was published in 2009 by the International Diabetes Federation (IDF) and the American Heart Association/National Heart, Lung, and Blood Institute (AHA/NHLBI) [39]. This "harmonized" definition shifted the diagnostic paradigm, removing any single obligatory component and establishing a flexible, coordinate-based system.

Under current clinical guidelines [40], the diagnosis of metabolic syndrome requires the presence of a basic diagnostic criterion combined with at least 2 out of 3 additional diagnostic criteria:

- Basic Criterion (Must be present): abdominal obesity (waist circumference ≥88 cm ≥102 cm in men) OR a body mass index (BMI) ≥30 kg/m^2
- Additional Criteria (At least 2 must be met):
  1. Prediabetes or diabetes: Fasting glucose ≥100 mg/dL OR glucose ≥140 mg/dL 120 minutes after an oral glucose tolerance test (OGTT) OR HbA_{1c} ≥5.7%, OR active glucose-lowering drug treatment.
  2. Elevated non-HDL cholesterol level: Non-HDL cholesterol ≥130 mg/dL, OR active lipid-lowering drug treatment.
  3. High normal blood pressure or hypertension: Blood pressure ≥130/85 mmHg (in-office measurement) OR ≥130/80 mmHg (home measurement) OR active anti-hypertensive treatment.

4. Implications of Metabolic Syndrome

The clinical implications of metabolic syndrome extend far beyond the traditional endpoints of cardiovascular events and type 2 diabetes, representing a systemic multisystem disorder. The chronic low-grade inflammation, insulin resistance, and visceral adiposity characteristic of the syndrome drive a wide array of secondary pathologies that significantly increase patient morbidity and complicate overall clinical management. Beyond these classical manifestations, metabolic syndrome may play a significant role in the onset and progression of metabolic dysfunction-associated steatotic liver disease and chronic renal dysfunction, while simultaneously inducing a prothrombotic state that drastically elevates the risk of vascular thrombosis [41]. Furthermore, the persistent low-grade inflammatory environment is increasingly recognized as a key trigger in the development and exacerbation of autoimmune diseases [42].

Ultimately, this cumulative burden of multi-organ dysfunction and systemic vascular damage dramatically accelerates overall disease progression, effectively doubling the risk of acute cardiovascular events and substantially increasing all-cause mortality [1].

5. Therapeutic Strategies: The Primacy of Lifestyle Modification

5.1. Nutritional Interventions and Dietary Patterns

Nutritional therapy is the cornerstone of non-pharmacological management in metabolic syndrome [43]. Rather than simple caloric restriction, clinical guidelines prioritize high-quality dietary patterns [44] — most notably the Mediterranean and DASH [45] diets.

The Mediterranean diet, rich in monounsaturated fatty acids (MUFAs), polyphenols, and marine-derived omega-3 polyunsaturated fatty acids (PUFAs), directly targets endothelial dysfunction by restoring nitric oxide bioavailability [46]. Simultaneously, PUFAs suppress the hepatic synthesis of very-low-density lipoproteins (VLDL) [47], actively lowering circulating triglycerides and shifting the atherogenic lipid triad toward a less pathogenic profile. Parallelly, the DASH diet — characterized by sodium restriction and high intake of potassium, magnesium, and calcium — directly mitigates arterial hypertension by reducing sympathetic tone and improving arterial compliance [48].

Beyond hemodynamics, these fibre-rich, plant-forward dietary patterns profoundly shape the gut microbiota. Enhanced bacterial fermentation of complex fibres increases the production of short-chain fatty acids (SCFAs), which fortify the intestinal mucosal barrier [49].

5.2. Physical Activity and Exercise

Structured physical activity and exercise function as powerful non-pharmacological therapies that directly counteract the pathophysiological core of metabolic syndrome [50]. Both aerobic and resistance training exert profound insulin-sensitizing effects by stimulating the translocation of glucose transporter 4 (GLUT-4) to the cell membrane of skeletal muscles via insulin-independent pathway [51]. This acutely bypasses receptor-level insulin resistance, lowering systemic glucose levels and reducing the pancreatic demand for insulin [52]. Furthermore, regular physical exercise serves as a major systemic anti-inflammatory stimulus [53]. Beyond metabolic and immunological reprogramming, exercise directly reverses vascular remodelling and reduces cardiovascular risk [54].

The mechanical shear stress induced by increased blood flow during exercise upregulates endothelial nitric oxide synthase activity, restoring nitric oxide bioavailability, improving endothelial function, and reducing arterial stiffness [55]. Simultaneously, exercise effectively dampens sympathetic nervous system overactivity, leading to a sustained reduction in resting blood pressure and heart rate [56]. By combining improved skeletal muscle insulin sensitivity, systemic anti-inflammatory signalling, and enhanced arterial compliance, regular exercise

directly targets and disrupts the self-perpetuating cycle of metabolic dysfunction, hypertension, and macrovascular damage.

5.3. Behavioural Strategies and Sleep Hygiene

Behavioural interventions and sleep hygiene are increasingly recognized as indispensable pillars in mitigating metabolic syndrome, directly targeting the neuroendocrine disruptions that drive its progression. Chronic psychological stress and sleep deprivation — defined as restricted sleep duration or poor sleep quality — exert a profound, synergistic impact on the hypothalamic-pituitary-adrenal axis and the sympathetic nervous system [57]. This chronic neuroendocrine overactivation leads to sustained hypercortisolaemia, which promotes visceral adiposity, impairs peripheral insulin sensitivity, and elevates blood pressure [58].

In contrast, structured behavioural strategies — such as mindfulness-based stress reduction, cognitive behavioural therapy for insomnia and the maintenance of a consistent circadian rhythm — effectively dampen hypothalamic-pituitary-adrenal axis reactivity [59]. By lowering circulating cortisol, restoring autonomic balance, and reducing systemic inflammatory tone, these behavioural and sleep-focused interventions may play a critical role in halting the self-perpetuating cycle of metabolic dysfunction, sympathovagal imbalance, and cardiovascular risk.

5.4. Pharmacological Interventions

Pharmacological management of metabolic syndrome is initiated when structured lifestyle modifications fail to adequately mitigate cardiometabolic risk, targeting individual components of the syndrome to disrupt their synergistic progression.

First-line therapy for hyperglycaemia and insulin resistance is historically anchored by metformin [60]. However, modern pharmacotherapy increasingly utilizes sodium-glucose cotransporter-2 (SGLT2) inhibitors and glucagon-like peptide-1 (GLP-1) receptor agonists due to their profound, organ-protective properties. GLP-1 receptor agonists enhance glucose-dependent insulin secretion, delay gastric emptying, and suppress appetite via hypothalamic signaling, driving significant visceral adiposity reduction and lowering systemic pro-inflammatory cytokines [61]. Simultaneously, SGLT2 inhibitors promote glucosuria, induce osmotic diuresis to lower blood pressure, and reduce sympathetic nervous system tone, directly mitigating arterial stiffness and offering robust cardiorenal protection [62].

To address the atherogenic lipid triad and prevent macrovascular events, HMG-CoA reductase inhibitors (statins) remain the clinical cornerstone, drastically reducing low-density lipoprotein

cholesterol (LDL-C) and stabilizing vulnerable atherosclerotic plaques [63]. When hypertriglyceridemia dominates, peroxisome proliferator-activated receptor-alpha agonists (fibrates) are utilized to lower circulating triglycerides and elevate high-density lipoprotein (HDL) levels.

Concurrently, arterial hypertension in metabolic syndrome is preferentially managed with renin-angiotensin-aldosterone system inhibitors, such as angiotensin-converting enzyme inhibitors or angiotensin II receptor blockers. By blocking the pro-inflammatory, vasoconstrictive, and hypertrophic pathways of angiotensin II, these pharmacotherapies not only lower blood pressure but also improve peripheral insulin sensitivity [64] and halt progressive structural remodelling of the arterial wall [65].

6. Conclusions

The metabolic syndrome represents one of the most critical public health challenges of the modern era, serving as a complex, multifaceted precursor to cardiovascular disease and type 2 diabetes. Rather than a collection of isolated clinical findings, the syndrome is a highly integrated pathophysiological state. At its core, sustained hyperinsulinemia and peripheral insulin resistance act as the primary metabolic drivers, triggering a cascade of downstream systemic disruptions. This includes the development of atherogenic dyslipidaemia — characterized by a qualitative and quantitative shift toward highly atherogenic small, dense LDL particles — and arterovascular changes that culminate in hypertension and progressive tissue damage long before overt clinical endpoints are diagnosed.

Fortunately, because metabolic syndrome is heavily rooted in overnutrition and physical inactivity, lifestyle modification remains the undisputed cornerstone of clinical management. Structured nutritional changes, such as the Mediterranean diet, combined with a precise prescription of both aerobic and resistance exercise, possess the unique physiological capacity to target and reverse the underlying insulin resistance. When implemented early and sustained long-term, these non-pharmacological interventions can halt the progression of the metabolic cascade, drastically reducing the patient's cardiovascular risk profile.

Concurrently, the therapeutic landscape has been revolutionized by the emergence of novel pharmacotherapies, specifically GLP-1 receptor agonists and dual GIP/GLP-1 receptor agonists. Originally designed to manage type 2 diabetes, these agents have demonstrated unprecedented efficacy in driving substantial weight loss, restoring metabolic homeostasis, and

directly mitigating cardiovascular mortality, thereby serving as a powerful, synergistic adjunct to foundational lifestyle interventions.

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References

[1] Mottillo S, Filion KB, Genest J, Joseph L, Pilote L, Poirier P, et al. The Metabolic Syndrome and Cardiovascular Risk: A Systematic Review and Meta-Analysis. Journal of the American College of Cardiology 2010;56:1113–32. https://doi.org/10.1016/j.jacc.2010.05.034.

[2] Drygas W, Bielecki W, Kozakiewicz K, Pajak A, Piotrowski W, Tykarski A, et al. Wieloośrodkowe Ogólnopolskie Badanie Stanu Zdrowia Ludności - WOBASZ, 2015, p. 41–55.

[3] Rajca A, Wojciechowska A, Śmigielski W, Drygas W, Piwońska A, Pająk A, et al. Increase in the prevalence of metabolic syndrome in Poland: comparison of the results of the WOBASZ (2003-2005) and WOBASZ II (2013-2014) studies. Polish Archives of Internal Medicine 2021;131:520–6. https://doi.org/10.20452/pamw.15975.

[4] Moore JX, Chaudhary N, Akinyemiju T. Metabolic Syndrome Prevalence by Race/Ethnicity and Sex in the United States, National Health and Nutrition Examination Survey, 1988–2012. Preventing Chronic Disease 2017;14. https://doi.org/10.5888/pcd14.160287.

[5] Dhondge RH, Agrawal S, Patil R, Kadu A, Kothari M. A Comprehensive Review of Metabolic Syndrome and Its Role in Cardiovascular Disease and Type 2 Diabetes Mellitus: Mechanisms, Risk Factors, and Management. Cureus 2024;16. https://doi.org/10.7759/cureus.67428.

[6] Wan H, Wang Y, Xiang Q, Fang S, Chen Y, Chen C, et al. Associations between abdominal obesity indices and diabetic complications: Chinese visceral adiposity index and neck circumference. Cardiovascular Diabetology 2020;19. https://doi.org/10.1186/s12933-020-01095-4.

[7] Trouwborst I, Bowser SM, Goossens GH, Blaak EE. Ectopic Fat Accumulation in Distinct Insulin Resistant Phenotypes; Targets for Personalized Nutritional Interventions. Frontiers in Nutrition 2018;5. https://doi.org/10.3389/fnut.2018.00077.

[8] Jia G, Aroor AR, DeMarco VG, Martinez-Lemus LA, Meininger GA, Sowers JR. Vascular stiffness in insulin resistance and obesity. Frontiers in Physiology 2015;6. https://doi.org/10.3389/fphys.2015.00231.

[9] Demetz G, Ott I. The Interface between Inflammation and Coagulation in Cardiovascular Disease. International Journal of Inflammation 2012;2012:1–8. https://doi.org/10.1155/2012/860301.

[10] Zwick RK, Guerrero-Juarez CF, Horsley V, Plikus MV. Anatomical, physiological and functional diversity of adipose tissue. Cell Metabolism 2018;27:68–83. https://doi.org/10.1016/j.cmet.2017.12.002.

[11] Yang Y-K, Chen M, Clements RH, Abrams GA, Aprahamian CJ, Harmon CM. Human mesenteric adipose tissue plays unique role versus subcutaneous and omental fat in obesity related diabetes. Cellular Physiology and Biochemistry : International Journal of Experimental Cellular Physiology, Biochemistry, and Pharmacology 2008;22:531–8. https://doi.org/10.1159/000185527.

[12] Lee M-J, Kim J. The pathophysiology of visceral adipose tissues in cardiometabolic diseases. Biochemical Pharmacology 2024;222:116116–6. https://doi.org/10.1016/j.bcp.2024.116116.

[13] Ibrahim MM. Subcutaneous and visceral adipose tissue: structural and functional differences. Obesity Reviews 2010;11:11–8. https://doi.org/10.1111/j.1467-789x.2009.00623.x.

[14] Saponaro C, Sabatini S, Gaggini M, Carli F, Rosso C, Positano V, et al. Adipose tissue dysfunction and visceral fat are associated with hepatic insulin resistance and severity of <scp>NASH</scp> even in lean individuals. Liver International 2022;42:2418–27. https://doi.org/10.1111/liv.15377.

[15] Kwok KHM, Lam KSL, Xu A. Heterogeneity of white adipose tissue: molecular basis and clinical implications. Experimental & Molecular Medicine 2016;48:e215–5. https://doi.org/10.1038/emm.2016.5.

[16] Little P, Offermanns S, Cho H, Liu Z, Yang P, Su Q, et al. Insulin Resistance: An Update on Biochemical and Pathophysiological Mechanisms and Impact on Various Diseases. iNew Medicine 2026. https://doi.org/10.1002/inm3.70028.

[17] Pliszka M, Szablewski L. Severe Insulin Resistance Syndromes: Clinical Spectrum and Management. International Journal of Molecular Sciences 2025;26:5669–9. https://doi.org/10.3390/ijms26125669.

[18] Boucher J, Kleinridders A, Kahn CR. Insulin Receptor Signaling in Normal and Insulin-Resistant States. Cold Spring Harbor Perspectives in Biology 2014;6:a009191–1. https://doi.org/10.1101/cshperspect.a009191.

[19] Thomas D D, Corkey BE, Istfan NW, Apovian CM. Hyperinsulinemia: An Early Indicator of Metabolic Dysfunction. Journal of the Endocrine Society 2019;3:1727–47. https://doi.org/10.1210/js.2019-00065.

[20] Manjunath C, Rawal J, Irani P, Madhu K. Atherogenic dyslipidemia. Indian Journal of Endocrinology and Metabolism 2013;17:969–76. https://doi.org/10.4103/2230-8210.122600.

[21] Austin MA, King MC, Vranizan KM, Krauss RM. Atherogenic lipoprotein phenotype. A proposed genetic marker for coronary heart disease risk. Circulation 1990;82:495–506. https://doi.org/10.1161/01.cir.82.2.495.

[22] Kazibwe R, Schaich CL, Chevli PA, Kingsley JA, Mirzai S, Namutebi JH, et al. Lipoprotein(a), Insulin Resistance, and Cardiovascular Disease in the UK Biobank. Journal of the American Heart Association 2026;15. https://doi.org/10.1161/jaha.125.042361.

[23] Marston NA, Giugliano RP, Melloni GEM, Park J-G, Morrill V, Blazing MA, et al. Association of Apolipoprotein B–Containing Lipoproteins and Risk of Myocardial Infarction in Individuals With and Without Atherosclerosis: Distinguishing Between Particle Concentration, Type, and Content. JAMA Cardiology 2022;7:250–6. https://doi.org/10.1001/jamacardio.2021.5083.

[24] Taskinen M-R, Borén J. New insights into the pathophysiology of dyslipidemia in type 2 diabetes. Atherosclerosis 2015;239:483–95. https://doi.org/10.1016/j.atherosclerosis.2015.01.039.

[25] Bekbossynova M, Saliev T, Ivanova-Razumova T, Andossova S, Kali A, Myrzakhmetova G. Small dense LDL: An underestimated driver of atherosclerosis (Review). Molecular Medicine Reports 2025;32:1–19. https://doi.org/10.3892/mmr.2025.13693.

[26] Moissl-Blanke AP, Delgado GE, Krämer BK, Siekmeier R, Duerschmied D, März W, et al. Serum Amyloid A (SAA) and Its Interaction with High-Density Lipoprotein Cholesterol (HDL-C): A Comprehensive Review. International Journal of Molecular Sciences 2025;27:241. https://doi.org/10.3390/ijms27010241.

[27] da Silva AA, do Carmo JM, Li X, Wang Z, Mouton AJ, Hall JE. Role of Hyperinsulinemia and Insulin Resistance in Hypertension: Metabolic Syndrome Revisited. Canadian Journal of Cardiology 2020;36:671–82. https://doi.org/10.1016/j.cjca.2020.02.066.

[28] Hall JE, do Carmo JM, da Silva AA, Wang Z, Hall ME. Obesity-Induced Hypertension. Circulation Research 2015;116:991–1006. https://doi.org/10.1161/circresaha.116.305697.

[29] Tziomalos K, Athyros VG, Karagiannis A, Mikhailidis DP. Endothelial dysfunction in metabolic syndrome: Prevalence, pathogenesis and management. Nutrition, Metabolism and Cardiovascular Diseases 2010;20:140–6. https://doi.org/10.1016/j.numecd.2009.08.006.

[30] Vanhoutte PM, Zhao Y, Xu A, Susan W.S. Leung. Thirty Years of Saying NO. Circulation Research 2016;119:375–96. https://doi.org/10.1161/circresaha.116.306531.

[31] Lacolley P, Regnault V, Laurent S. Mechanisms of Arterial Stiffening: From Mechanotransduction to Epigenetics. Arteriosclerosis, Thrombosis, and Vascular Biology 2020;40:1055–62. https://doi.org/10.1161/ATVBAHA.119.313129.

[32] Laurent S, Boutouyrie P. Arterial stiffness: a new surrogate end point for cardiovascular disease? Journal of Nephrology 2007;20 Suppl 12:S45-50.

[33] Chait A, den Hartigh LJ. Adipose Tissue Distribution, Inflammation and Its Metabolic Consequences, Including Diabetes and Cardiovascular Disease. Frontiers in Cardiovascular Medicine 2020;7. https://doi.org/10.3389/fcvm.2020.00022.

[34] Reilly SM, Saltiel AR. Adapting to obesity with adipose tissue inflammation. Nature Reviews Endocrinology 2017;13:633–43. https://doi.org/10.1038/nrendo.2017.90.

[35] Achari AE, Jain SK. Adiponectin, a Therapeutic Target for Obesity, Diabetes, and Endothelial Dysfunction. International Journal of Molecular Sciences 2017;18:1321. https://doi.org/10.3390/ijms18061321.

[36] Bou Matar D, Zhra M, Nassar WK, Altemyatt H, Naureen A, Abotouk N, et al. Adipose tissue dysfunction disrupts metabolic homeostasis: mechanisms linking fat dysregulation to disease. Frontiers in Endocrinology 2025;16. https://doi.org/10.3389/fendo.2025.1592683.

[37] Alessi M-C, Juhan-Vague I. PAI-1 and the Metabolic Syndrome. Arteriosclerosis, Thrombosis, and Vascular Biology 2006;26:2200–7. https://doi.org/10.1161/01.atv.0000242905.41404.68.

[38] Huilcaman R, Venturini W, Fuenzalida L, Cayo A, Segovia R, Valenzuela C, et al. Platelets, a Key Cell in Inflammation and Atherosclerosis Progression. Cells 2022;11:1014. https://doi.org/10.3390/cells11061014.

[39] Alberti KGMM, Eckel RH, Grundy SM, Zimmet PZ, Cleeman JI, Donato KA, et al. Harmonizing the metabolic syndrome: A joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity. Circulation 2009;120:1640–5. https://doi.org/10.1161/CIRCULATIONAHA.109.192644.

[40] Dobrowolski P, Prejbisz A, Kuryłowicz A, Baska A, Burchardt P, Chlebus K, et al. Metabolic syndrome – A new definition and management guidelines. Archives of Medical Science 2022;18:1133–56. https://doi.org/10.5114/aoms/152921.

[41] Rochlani Y, Pothineni NV, Kovelamudi S, Mehta JL. Metabolic syndrome: pathophysiology, management, and modulation by natural compounds. Therapeutic Advances in Cardiovascular Disease 2017;11:215–25. https://doi.org/10.1177/1753944717711379.

[42] Versini M, Jeandel P-Y, Rosenthal E, Shoenfeld Y. Obesity in autoimmune diseases: Not a passive bystander. Autoimmunity Reviews 2014;13:981–1000. https://doi.org/10.1016/j.autrev.2014.07.001.

[43] Evert AB, Dennison M, Gardner CD, Garvey WT, Lau KHK, MacLeod J, et al. Nutrition Therapy for Adults With Diabetes or Prediabetes: A Consensus Report. Diabetes Care 2019;42:731–54. https://doi.org/10.2337/dci19-0014.

[44] Fahed G, Aoun L, Bou Zerdan M, Allam S, Bou Zerdan M, Bouferraa Y, et al. Metabolic Syndrome: Updates on Pathophysiology and Management in 2021. International Journal of Molecular Sciences 2022;23:786. https://doi.org/10.3390/ijms23020786.

[45] Soltani S, Shirani F, Chitsazi MJ, Salehi-Abargouei A. The effect of dietary approaches to stop hypertension (DASH) diet on weight and body composition in adults: a systematic review and meta-analysis of randomized controlled clinical trials. Obesity Reviews 2016;17:442–54. https://doi.org/10.1111/obr.12391.

[46] Shannon OM, Stephan BCM, Minihane A-M, Mathers JC, Siervo M. Nitric Oxide Boosting Effects of the Mediterranean Diet: A Potential Mechanism of Action. The Journals of Gerontology Series A, Biological Sciences and Medical Sciences 2018;73:902–4. https://doi.org/10.1093/gerona/gly087.

[47] Backes J, Anzalone D, Hilleman D, Catini J. The clinical relevance of omega-3 fatty acids in the management of hypertriglyceridemia. Lipids in Health and Disease 2016;15. https://doi.org/10.1186/s12944-016-0286-4.

[48] Sacks FM, Svetkey LP, Vollmer WM, Appel LJ, Bray GA, Harsha D, et al. Effects on blood pressure of reduced dietary sodium and the dietary approaches to stop hypertension (DASH) diet. DASH-Sodium Collaborative Research Group. The New England Journal of Medicine 2001;344:3–10. https://doi.org/10.1056/NEJM200101043440101.

[49] Parada Venegas D, De la Fuente MK, Landskron G, González MJ, Quera R, Dijkstra G, et al. Short Chain Fatty Acids (SCFAs)-Mediated Gut Epithelial and Immune Regulation and Its Relevance for Inflammatory Bowel Diseases. Frontiers in Immunology 2019;10. https://doi.org/10.3389/fimmu.2019.00277.

[50] Myers J, Kokkinos P, Nyelin E. Physical Activity, Cardiorespiratory Fitness, and the Metabolic Syndrome. Nutrients 2019;11:1652. https://doi.org/10.3390/nu11071652.

[51] Richter EA, Hargreaves M. Exercise, GLUT4, and Skeletal Muscle Glucose Uptake. Physiological Reviews 2013;93:993–1017. https://doi.org/10.1152/physrev.00038.2012.

[52] Sylow L, Kleinert M, Richter EA, Jensen TE. Exercise-stimulated Glucose Uptake — Regulation and Implications for Glycaemic Control. Nature Reviews Endocrinology 2016;13:133–48. https://doi.org/10.1038/nrendo.2016.162.

[53] Gleeson M, Bishop NC, Stensel DJ, Lindley MR, Mastana SS, Nimmo MA. The anti-inflammatory effects of exercise: mechanisms and implications for the prevention and

treatment of disease. Nature Reviews Immunology 2011;11:607–15. https://doi.org/10.1038/nri3041.

[54] Green DJ, Hopman MTE, Padilla J, Laughlin MH, Thijssen DHJ. Vascular Adaptation to Exercise in Humans: Role of Hemodynamic Stimuli. Physiological Reviews 2017;97:495–528. https://doi.org/10.1152/physrev.00014.2016.

[55] Laughlin MH, Davis MJ, Secher NH, Lieshout JJ, Arce-Esquivel AA, Simmons GH, et al. Peripheral Circulation. Comprehensive Physiology 2012;2:321–447. https://doi.org/10.1002/cphy.c100048.

[56] Cornelissen VA, Smart NA. Exercise Training for Blood Pressure: A Systematic Review and Meta-analysis. Journal of the American Heart Association 2013;2. https://doi.org/10.1161/jaha.112.004473.

[57] Leproult R, Van Cauter E. Role of sleep and sleep loss in hormonal release and metabolism. Pediatric Neuroendocrinology 2009;17:11–21. https://doi.org/10.1159/000262524.

[58] McEwen BS, Karatsoreos IN. Sleep Deprivation and Circadian Disruption Stress, Allostasis, and Allostatic Load. Sleep Medicine Clinics 2022. https://doi.org/10.1016/j.jsmc.2022.03.005.

[59] Mc P, Dr T, Cf S. Yoga, Mindfulness-Based Stress Reduction and Stress-Related Physiological Measures: A Meta-Analysis. Psychoneuroendocrinology 2017. https://pubmed.ncbi.nlm.nih.gov/28963884/ (accessed July 15, 2026).

[60] American Diabetes Association . Pharmacologic Approaches to Glycemic Treatment: Standards of Medical Care in Diabetes—2020. Diabetes Care 2020;43:S98–110. https://doi.org/10.2337/dc20-s009.

[61] Baggio LL, Drucker DJ. Glucagon-like peptide-1 receptor co-agonists for treating metabolic disease. Molecular Metabolism 2021;46:101090. https://doi.org/10.1016/j.molmet.2020.101090.

[62] Wang A, Li Z, Zhuo S, Gao F, Zhang H, Zhang Z, et al. Mechanisms of Cardiorenal Protection With SGLT2 Inhibitors in Patients With T2DM Based on Network Pharmacology. Frontiers in Cardiovascular Medicine 2022;9. https://doi.org/10.3389/fcvm.2022.857952.

[63] Libby P. Current Concepts of the Pathogenesis of the Acute Coronary Syndromes. Circulation 2001;104:365–72. https://doi.org/10.1161/01.cir.104.3.365.

[64] Scheen A. Renin-angiotensin system inhibition prevents type 2 diabetes mellitus. Diabetes & Metabolism 2004;30:498–505. https://doi.org/10.1016/s1262-3636(07)70147-7.

[65] Savoia C, Schiffrin EL. Inhibition of the renin angiotensin system: implications for the endothelium. Current Diabetes Reports 2006;6:274–8. https://doi.org/10.1007/s11892-006-0060-5.