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CHEMICAL REMODELING OF THE BLOOD METABOLOME DURING MENOPAUSE AND ITS ASSOCIATION WITH CARDIOVASCULAR DISEASE RISK

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Abstract

Menopause is accompanied by profound endocrine, metabolic, and biochemical alterations that affect the composition and function of circulating blood. The decline in ovarian estrogen production is associated with changes in lipid metabolism, lipoprotein composition, glucose homeostasis, amino-acid metabolism, fatty-acid oxidation, inflammation, and oxidative stress. These metabolic alterations may contribute substantially to the increasing cardiovascular disease risk observed in women during and after the menopausal transition.This narrative review analyzes current scientific evidence concerning menopause-associated changes in the chemical composition of blood and their relationship with cardiovascular disease. Particular attention is given to alterations in conventional lipid parameters, lipoprotein subclasses, apolipoprotein B, triglyceride-rich lipoproteins, fatty acids, amino acids, glucose-related metabolites, inflammatory biomarkers, and oxidative stress markers. The potential contribution of modern analytical approaches, including nuclear magnetic resonance spectroscopy, mass spectrometry, metabolomics, and lipidomics, is also considered.Available evidence indicates that menopause is associated with a shift toward a more atherogenic circulating biochemical profile, characterized by increased concentrations of low-density lipoprotein cholesterol, apolipoprotein B, triglycerides, and several very-low-density lipoprotein subclasses. At the same time, changes in amino acids, fatty-acid metabolites, ketone bodies, glycerol, and intermediary metabolites indicate that menopause represents a broader metabolic transition rather than an isolated alteration in lipid metabolism.Understanding menopause-associated chemical remodeling of the blood metabolome may contribute to the identification of novel biomarkers for early cardiovascular risk assessment. Integration of conventional biochemical analysis with metabolomic and lipidomic approaches may provide a more comprehensive understanding of cardiovascular disease mechanisms in postmenopausal women.

Keywords: menopause, cardiovascular disease, blood metabolome, lipidomics, metabolomics, lipoproteins, apolipoprotein B, estrogen deficiency, oxidative stress, biomarkers.

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Introduction

Menopause represents a major physiological transition characterized by cessation of ovarian function and a substantial decline in circulating estrogen concentrations. These endocrine changes initiate a complex series of metabolic adaptations involving lipid metabolism, glucose regulation, adipose tissue distribution, vascular function, and inflammatory pathways.The cardiovascular system is particularly sensitive to these changes. Before menopause, women generally demonstrate a lower incidence of cardiovascular disease compared with age-matched men. However, cardiovascular risk increases progressively during the menopausal transition and after menopause. This phenomenon is associated not only with chronological aging but also with changes in endocrine and metabolic regulation.

From the perspective of biochemistry and analytical chemistry, menopause is accompanied by measurable modifications in the chemical composition of blood. These include alterations in cholesterol and triglyceride concentrations, lipoprotein particle distribution, apolipoproteins, fatty acids, amino acids, glucose-related metabolites, inflammatory mediators, and markers of oxidative stress.

Traditional laboratory assessment usually focuses on total cholesterol, LDL-C, HDL-C, triglycerides, glucose, and selected inflammatory markers. Although these parameters remain clinically important, they provide only a limited representation of the circulating metabolic environment.

Modern metabolomic and lipidomic technologies allow simultaneous analysis of hundreds or thousands of chemically distinct molecules. These approaches have demonstrated that menopause is associated with coordinated remodeling of multiple metabolic pathways. Consequently, characterization of the blood metabolome may provide new insights into the mechanisms connecting estrogen deficiency with cardiovascular disease.

Endocrine Basis of Metabolic Remodeling During Menopause

Estrogen is an important regulator of systemic metabolism. It influences hepatic lipid metabolism, adipose tissue function, glucose homeostasis, vascular endothelial signaling, and inflammatory responses.

During reproductive life, ovarian estrogen contributes to the maintenance of a relatively favorable metabolic profile. With the decline in ovarian estrogen production during menopause, several metabolic pathways become altered.

The principal endocrine changes include:

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- reduction in circulating estradiol;
- altered estrogen receptor signaling;
- changes in hepatic lipid metabolism;
- redistribution of adipose tissue toward visceral deposition;
- changes in insulin sensitivity;
- increased inflammatory activity;
- alterations in vascular endothelial function.

These processes interact with each other and contribute to remodeling of the circulating biochemical profile.

The transition can therefore be represented as:

Estrogen deficiency → metabolic remodeling → altered blood chemistry → vascular dysfunction → increased cardiovascular risk.

This process demonstrates why biochemical investigation of menopause should include multiple metabolic pathways rather than a single laboratory parameter.

Changes in the Lipid Composition of Blood During Menopause

One of the most consistently documented biochemical consequences of menopause is alteration of lipid metabolism.

The principal changes include:

- increased total cholesterol;
- increased LDL-C;
- increased triglycerides;
- increased apoB;
- increased concentrations of triglyceride-rich lipoproteins;
- alterations in HDL composition;
- changes in LDL and VLDL particle subclasses.

Prospective studies indicate that several of these changes become particularly evident around the final menstrual period. The increase in atherogenic lipoproteins contributes to the development of an unfavorable cardiovascular risk profile.

However, the concentration of total cholesterol alone does not adequately describe these changes. The distribution of cholesterol among different lipoprotein particles is biologically important because individual particles differ in their ability to participate in atherogenesis.

Low-Density Lipoproteins and Atherogenicity

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Low-density lipoproteins are the principal carriers of cholesterol from the liver to peripheral tissues. Increased concentrations of circulating LDL particles are strongly associated with atherosclerotic cardiovascular disease.

During menopause, LDL-C generally increases, accompanied in many women by an increase in LDL particle concentration.

The biochemical importance of LDL extends beyond its cholesterol content. LDL particles can enter the arterial intima and undergo chemical modifications, including oxidation. Modified LDL may subsequently interact with macrophages and contribute to foam-cell formation.

The process can be summarized as:

↑ LDL particles → arterial penetration → oxidative modification → macrophage uptake → foam-cell formation → atherosclerotic plaque.

Therefore, menopause-associated elevation of LDL-related parameters represents an important component of cardiovascular risk.

Apolipoprotein B and Atherogenic Particle Number

Apolipoprotein B represents one of the most informative biochemical markers of atherogenic lipoprotein particle concentration.

Each circulating atherogenic lipoprotein particle generally contains one apoB molecule. Consequently, apoB reflects the number of potentially atherogenic particles rather than simply the amount of cholesterol transported within them.

Menopause is associated with increased apoB concentrations in many women. This finding is particularly important because two individuals may have similar LDL-C concentrations but different numbers of LDL particles and therefore different atherogenic burdens.

From an analytical chemistry perspective, apoB may therefore provide complementary information to conventional cholesterol measurements.

The integration of:

LDL-C + non-HDL-C + apoB + triglyceride-rich lipoproteins

may provide a more complete characterization of the atherogenic blood profile during menopause.

Triglycerides and Very-Low-Density Lipoproteins

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Triglycerides constitute an important component of circulating lipoproteins, particularly VLDL and other triglyceride-rich particles.

Menopause may be associated with increased hepatic production and altered clearance of triglyceride-rich lipoproteins. Consequently, plasma triglyceride concentrations and VLDL-related parameters may increase.

Elevated triglycerides are particularly important when combined with:

- visceral obesity;
- insulin resistance;
- elevated glucose;
- low or dysfunctional HDL;
- increased apoB.

This combination represents a characteristic metabolic environment associated with increased cardiovascular risk.

The chemical remodeling of triglyceride-rich lipoproteins may also promote the formation of remnant particles that are capable of contributing directly to atherosclerotic plaque formation.

HDL Metabolism and Functional Alterations

High-density lipoproteins have traditionally been considered protective because of their involvement in reverse cholesterol transport.

However, modern biochemical research indicates that HDL concentration alone does not fully characterize HDL function.

During menopause, HDL particle composition and functionality may change. These alterations may involve:

- particle size;
- particle number;
- triglyceride content;
- phospholipid composition;
- cholesterol efflux capacity;
- antioxidant properties.

Consequently, the measurement of HDL-C alone may be insufficient for understanding changes in HDL biology during menopause.

Future studies should investigate not only HDL-C concentration but also the molecular composition and functional properties of HDL particles.

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Fatty Acids and Lipid Mediators

Fatty acids represent major components of plasma lipids and are essential substrates for energy metabolism and membrane synthesis.

Menopause-associated changes in body composition and insulin sensitivity may influence fatty-acid mobilization and oxidation.

Alterations may occur in:

- saturated fatty acids;
- monounsaturated fatty acids;
- polyunsaturated fatty acids;
- phospholipid-associated fatty acids;
- acylcarnitines;
- oxidized lipid mediators.

Changes in these molecules may reflect disturbances in mitochondrial energy metabolism and lipid oxidation.

Particularly important are lipid mediators derived from polyunsaturated fatty acids. These compounds participate in inflammatory and vascular signaling and may influence endothelial function.

Thus, lipidomics may provide information about cardiovascular risk that cannot be obtained from conventional triglyceride or cholesterol measurements alone.

Amino-Acid Metabolism During Menopause

The blood metabolome includes numerous amino acids that participate in energy metabolism, protein synthesis, cellular signaling, and vascular regulation.

Menopause-associated metabolic changes may affect concentrations of:

- leucine;
- isoleucine;
- valine;
- glycine;
- glutamate;
- phenylalanine;
- tyrosine;
- arginine;
- other amino-acid metabolites.

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Branched-chain amino acids are particularly relevant because their metabolism is associated with insulin resistance and metabolic syndrome.

Altered amino-acid profiles may therefore represent biochemical indicators of metabolic dysfunction accompanying menopause.

In addition, metabolites involved in arginine and nitric oxide metabolism may influence vascular endothelial function and contribute to cardiovascular pathology.

Glucose Metabolism and Insulin Resistance

Menopause is frequently accompanied by redistribution of adipose tissue toward visceral accumulation. This process is closely associated with insulin resistance.

Insulin resistance results in a characteristic biochemical pattern involving:

- increased fasting insulin;
- impaired glucose regulation;
- increased triglycerides;
- altered fatty-acid metabolism;
- increased inflammatory activity.

Hyperinsulinemia may also influence hepatic lipoprotein metabolism and promote the production of triglyceride-rich particles.

The interaction between glucose and lipid metabolism is therefore particularly important in understanding cardiovascular risk during menopause.

A simplified biochemical relationship can be represented as:

Estrogen deficiency → visceral adiposity → insulin resistance → hyperinsulinemia → dyslipidemia → cardiovascular risk.

Chronic Inflammation and Blood Biochemistry

Chronic low-grade inflammation is another important component of menopause-associated metabolic remodeling.

Inflammatory mediators may include:

- high-sensitivity C-reactive protein;
- interleukin-6;
- tumor necrosis factor-α;
- fibrinogen;
- chemokines;

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- endothelial adhesion molecules.

Adipose tissue contributes substantially to systemic inflammation by releasing adipokines and cytokines.

Inflammation can interact with lipid abnormalities to accelerate endothelial dysfunction and atherosclerosis.

Thus, the cardiovascular risk associated with menopause should be understood as the result of interactions between **lipid abnormalities, metabolic dysfunction and inflammation**.

Oxidative Stress and Chemical Modification of Biomolecules

Oxidative stress occurs when the production of reactive oxygen species exceeds antioxidant defense capacity.

During menopause, changes in estrogen signaling, adiposity, mitochondrial metabolism, and inflammation may contribute to increased oxidative stress.

Reactive oxygen species can chemically modify:

- lipids;
- proteins;
- nucleic acids;
- lipoproteins;
- cellular membranes.

Oxidized LDL is particularly relevant to atherogenesis. It can stimulate inflammatory responses and promote macrophage lipid accumulation.

Potential biochemical indicators include:

- oxidized LDL;
- malondialdehyde;
- lipid peroxidation products;
- protein carbonyls;
- F2-isoprostanes;
- antioxidant capacity.

The integration of oxidative-stress biomarkers with lipidomic data could provide a more detailed description of cardiovascular risk.

Metabolomics and Lipidomics in Menopausal Research

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Modern analytical chemistry provides tools capable of characterizing the complex chemical composition of blood.

Metabolomics investigates large numbers of low-molecular-weight metabolites simultaneously.

Lipidomics focuses specifically on the molecular diversity of lipids and lipid-derived mediators.

The principal analytical technologies include:

- nuclear magnetic resonance spectroscopy;
- liquid chromatography–mass spectrometry;
- gas chromatography–mass spectrometry;
- tandem mass spectrometry;
- high-resolution mass spectrometry.

These technologies enable detection of metabolic changes that remain invisible to conventional biochemical testing.

Recent prospective studies have demonstrated that menopause is associated with a distinct circulating metabolomic profile involving lipoproteins, fatty acids, amino acids, glycerol, ketone bodies, and intermediary metabolites.

This supports the concept that menopause produces **systemic chemical remodeling of the blood metabolome** rather than isolated changes in cholesterol.

Integrated Biochemical Model of Cardiovascular Risk

The interaction between menopause and cardiovascular disease can be represented by an integrated biochemical model:

Declining estrogen

↓

Altered hepatic and adipose-tissue metabolism

↓

Visceral adiposity + insulin resistance

↓

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↑ VLDL + ↑ triglycerides + ↑ LDL/apoB

↓

Altered HDL composition

↓

Oxidative stress + chronic inflammation

↓

Endothelial dysfunction

↓

Atherosclerosis

↓

Cardiovascular disease

This model emphasizes that the cardiovascular consequences of menopause arise from several interconnected biochemical pathways.

Clinical and Analytical Implications

The coexistence of menopause-associated endocrine changes and metabolic abnormalities has important implications for cardiovascular risk assessment.

Women during and after menopause may demonstrate:

- increased LDL-C;
- increased apoB;
- increased triglycerides;
- altered VLDL metabolism;
- changes in HDL composition;
- increased visceral adiposity;
- insulin resistance;
- increased inflammatory activity;
- altered amino-acid metabolism;
- changes in fatty-acid metabolism.

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Conventional biochemical assessment should therefore be complemented, where appropriate, by advanced molecular approaches.

A future cardiovascular risk panel for postmenopausal women could potentially integrate:

Lipid profile + apoB + Lp(a) + glucose/insulin + inflammatory markers + selected metabolites + lipidomic profile.

Such an approach may provide a more individualized biochemical assessment of cardiovascular risk.

Preventive Perspectives

Prevention should focus on modification of metabolic factors that contribute to adverse blood chemistry.

Important measures include:

- maintenance of healthy body weight;
- regular physical activity;
- balanced nutrition;
- adequate intake of dietary fiber and unsaturated fatty acids;
- control of blood glucose;
- optimization of lipid parameters;
- blood pressure control;
- reduction of smoking and other cardiovascular risk factors;
- monitoring of metabolic biomarkers.

From a biochemical perspective, preventive strategies should aim not only to reduce LDL-C but also to improve the overall metabolic environment characterized by lipid balance, insulin sensitivity and reduced chronic inflammation.

Future Perspectives

Future research should investigate menopause-associated cardiovascular risk using multidimensional chemical profiling.

A particularly promising research strategy would combine:

sex hormones + conventional blood chemistry + lipidomics + metabolomics + inflammatory biomarkers + cardiovascular phenotype.

Such an approach could identify molecular signatures associated with different stages of menopausal transition.

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Machine-learning methods could subsequently be applied to identify combinations of metabolites capable of predicting:

1. metabolic syndrome;
2. subclinical atherosclerosis;
3. coronary artery disease;
4. cardiovascular events;
5. accelerated metabolic aging.

The identification of such molecular signatures could potentially lead to earlier and more individualized cardiovascular prevention.

Conclusion

Menopause represents a major endocrine-metabolic transition associated with significant chemical remodeling of the blood metabolome. Estrogen deficiency affects lipid transport, lipoprotein metabolism, glucose homeostasis, fatty-acid oxidation, amino-acid metabolism, inflammation, and oxidative balance.

The most clinically recognized changes include increased LDL-C, triglycerides and apoB, together with alterations in VLDL and HDL metabolism. However, metabolomic and lipidomic studies demonstrate that these changes occur within a much broader network of biochemical alterations involving fatty acids, amino acids, glycerol, ketone bodies, phospholipids and other intermediary metabolites.

The interaction between these biochemical pathways may contribute to endothelial dysfunction, atherosclerosis and the increased cardiovascular disease risk observed after menopause.

Therefore, investigation of the **chemical composition of blood and its metabolomic remodeling during menopause** represents a promising direction for modern cardiovascular and analytical chemistry research. Integration of conventional biochemical markers with NMR spectroscopy, mass spectrometry, metabolomics and lipidomics may improve understanding of disease mechanisms and facilitate the discovery of novel biomarkers for early cardiovascular risk assessment.

References

1. Matthews K.A., Crawford S.L., Chae C.U., et al. Are changes in cardiovascular disease risk factors in midlife women due to chronological aging or to the menopausal transition? *Archives of Internal Medicine*. 2009.
2. Wildman R.P., Colvin A.B., Powell L.H., et al. Associations of endogenous sex hormones with lipids and lipoproteins in postmenopausal women. *Journal of Clinical Endocrinology & Metabolism*.

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3. Anagnostis P., Stevenson J.C., Goulis D.G., et al. Cardiovascular health and the menopause. *Best Practice & Research Clinical Endocrinology & Metabolism*. 2024.
4. Uddenberg E.R., Safwan N., Saadedine M., et al. Menopause transition and cardiovascular disease risk. *Maturitas*. 2024;185:107974.
5. Johannesen C.D.L., Langsted A., Nordestgaard B.G., Mortensen M.B. Excess apolipoprotein B and cardiovascular risk in women and men. *Journal of the American College of Cardiology*. 2024;83:2262–2273.
6. Mozaffarian D., et al. Menopause modulates the circulating metabolome: evidence from a prospective cohort study. 2022.
7. Balasubramanian R., Demler O., Guasch-Ferré M., et al. Metabolomic effects of hormone therapy and associations with coronary heart disease among postmenopausal women. *Circulation: Genomic and Precision Medicine*. 2020;13:e002977.
8. Anagnostis P., et al. The effect of menopause on lipoprotein(a) concentrations: a systematic review and meta-analysis. *Maturitas*. 2022.
9. Takebayashi T., et al. Metabolic profiling of charged metabolites in association with menopausal status in Japanese community-dwelling midlife women. *Maturitas*. 2021.
10. Evaluating the association between amino acid and acylcarnitine profiles and different levels of coronary artery disease risk in postmenopausal women using targeted metabolomics. 2022.
11. Wang Q., Xie B., Fu C., et al. Integrating menopause duration and plasma metabolomics enhances cardiovascular risk stratification in aging women. *npj Aging*. 2026.
12. Santen R.J., Yue W., Wang J.P., Fan P. Estrogen metabolism and breast cancer. *Journal of Steroid Biochemistry and Molecular Biology*. 2020;204:105754.
13. Alberti K.G.M.M., Eckel R.H., Grundy S.M., et al. Harmonizing the metabolic syndrome. *Circulation*. 2009;120:1640–1645.
14. Lovejoy J.C., Champagne C.M., de Jonge L., et al. Increased visceral fat and decreased energy expenditure during menopause. *Journal of Clinical Endocrinology & Metabolism*. 2008;93:4232–4238.
15. Rose D.P., Vona-Davis L. Biochemical and molecular mechanisms linking obesity and breast cancer. *Endocrine-Related Cancer*. 2014;21:R365–R384.