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EVALUATION OF LIPID SPECTRUM INDICATORS IN ATHEROSCLEROTIC RENAL ARTERY DISEASE

Nazarova Nigina Otabekovna – Ph.D.
Tashkent State Medical University (Tashkent, Uzbekistan)

Annotation. *Atherosclerosis of the renal arteries is a significant contributor to renovascular hypertension and kidney dysfunction. Dyslipidaemia is a recognized risk factor for atherosclerosis in general, yet specific data on the lipid-spectrum changes in renal artery atherosclerosis are less extensive. This article reviews current research on lipid spectrum indicators (including total cholesterol, LDL-cholesterol, HDL-cholesterol, triglycerides, apolipoproteins and lipoprotein(a) in patients with atherosclerotic renal artery disease, discusses their potential value for assessment and risk stratification, and highlights gaps and future research directions. Evidence suggests that some lipid parameters (such as lower apoA1, altered apoA1/apoB ratio, higher Lp(a) in certain contexts) may be associated with renal artery atherosclerosis. Standard lipid-panel measures alone may not fully capture the residual risk in this population. Further well-designed studies are needed to define the optimal lipid spectrum indicators for renal artery disease and to integrate them into clinical assessment.*

Key words*: Atherosclerotic renal artery stenosis, dyslipidaemia, LDL-cholesterol.*

ОЦЕНКА ПОКАЗАТЕЛЕЙ ЛИПИДНОГО СПЕКТРА ПРИ АТЕРОСКЛЕРОТИЧЕСКОМ ПОРАЖЕНИИ ПОЧЕЧНЫХ АРТЕРИЙ

Назарова Нигина Отабековна – Ph.D.
Ташкентский государственный медицинский университет (Ташкент, Узбекистан)

Аннотация. *Атеросклероз почечных артерий является важным фактором развития реноваскулярной гипертензии и нарушения функции почек. Дислипидемия признана одним из ключевых факторов риска атеросклероза в целом, однако специфические данные об изменениях липидного спектра при атеросклерозе почечных артерий изучены недостаточно. В данной статье рассматриваются современные исследования показателей липидного спектра (включая общий холестерин, липопротеины низкой плотности (ЛПНП), липопротеины высокой плотности (ЛПВП), триглицериды, аполипопротеины и липопротеин(а) у пациентов с атеросклеротическим поражением почечных артерий, обсуждается их потенциальная роль в оценке и стратификации риска, а также обозначаются существующие пробелы и направления для будущих исследований. Согласно имеющимся данным, некоторые параметры липидного обмена (такие как снижение уровня апоА1, изменение соотношения апоА1/апоВ, повышение уровня Lp(a) в определённых условиях) могут быть связаны с атеросклерозом почечных артерий. Стандартные показатели липидного профиля не всегда позволяют в полной мере оценить остаточный риск у данной категории пациентов. Необходимы дальнейшие хорошо спланированные исследования для определения оптимальных показателей липидного спектра при атеросклеротическом поражении почечных артерий и их интеграции в клиническую практику.*

Ключевые слова: *атеросклеротический стеноз почечных артерий, дислипидемия, липопротеины низкой плотности (ЛПНП).*

BUYRAK ARTERIYALARI ATEROSKLEROZIDA LIPID SPEKTRI KO‘RSATKICHLARINI BAHOLASH

Nazarova Nigina Otabek qizi – Ph.D.
Toshkent davlat tibbiyot universiteti (Toshkent, O‘zbekiston)

Annotatsiya. *Buyrak arteriyalarining aterosklerozi buyrak qon tomir gipertenziyasi va buyrak faoliyatining buzilishiga olib keluvchi muhim omillardan biridir. Dislipidemiya umuman olganda aterosklerozning asosiy xavf omillaridan biri sifatida tan olingan bo‘lsa-da, buyrak arteriyalarining aterosklerozida lipid spektri o‘zgarishlari bo‘yicha ma’lumotlar yetarlicha o‘rganilmagan. Ushbu maqolada bemorlarda buyrak arteriyalarining aterosklerotik kasalliklarida lipid spektri ko‘rsatkichlari (umumiy xolesterin, past zichlikdagi lipoproteinlar (LDL-xolesterin), yuqori zichlikdagi lipoproteinlar (HDL-xolesterin), triglitseridlar, apolipoproteinlar va lipoprotein(a) [Lp(a)]) haqidagi*

so‘nggi ilmiy tadqiqotlar tahlil qilinadi. Shuningdek, ushbu ko‘rsatkichlarning baholash va xavfni aniqlashdagi ahamiyati, mavjud bo‘shliqlar hamda kelgusidagi ilmiy yo‘nalishlari muhokama qilinadi. Tadqiqotlar shuni ko‘rsatadiki, ayrim lipid ko‘rsatkichlari (masalan, apolipoprotein A1 darajasining pasayishi, apolipoprotein A1/apolipoprotein B nisbatining o‘zgarishi, ba’zi hollarda Lp(a) darajasining oshishi) buyrak arteriyalarining aterosklerozi bilan bog‘liq bo‘lishi mumkin. Standart lipid paneli ko‘rsatkichlari ushbu guruhdagi bemorlarda to‘liq xavfni aniqlash imkonini bermasligi mumkin. Shu bois, lipid spektrining optimal ko‘rsatkichlarini aniqlash va ularni klinik baholash tizimiga kiritish uchun chuqur o‘ylangan tadqiqotlar o‘tkazish zarur.

Kalit so‘zlar: *buyrak arteriyasi aterosklerotik stenozi, dislipidemiya, past zichlikdagi lipoprotein (LDL-xolesterin).*

Introduction.

Atherosclerotic involvement of the renal arteries (commonly referred to as atherosclerotic renal artery stenosis, ARAS) is a prevalent condition, particularly in older adults and those with hypertension, diabetes or established systemic atherosclerosis [1]. The pathophysiology involves lipid deposition in the intima, endothelial dysfunction, smooth muscle proliferation, inflammation and subsequent luminal narrowing. Hyperlipidaemia (elevated total cholesterol, LDL-C, and triglycerides; low HDL-C) is a well-established risk factor for atherosclerosis in coronary and peripheral arteries. However, the specific relationships between the full lipid spectrum (including apolipoprotein levels and lipoprotein(a)) and renal artery atherosclerosis are less clear [2].

Given the increasing burden of ARAS and its implications for renal and cardiovascular outcomes, there is interest in understanding whether additional lipid markers beyond the traditional panel might help in risk stratification, early detection and targeted therapy of renal artery atherosclerosis. This article aims to summarise current evidence for lipid spectrum indicators in renal artery atherosclerosis, highlight key findings and limitations, and propose considerations for clinical and research use [3,9].

Pathophysiology of Atherosclerosis in the Renal Arteries and the Role of Lipids

The mechanism of atherosclerosis in the renal artery parallels that in other large arteries: endothelial injury, retention of atherogenic lipoproteins (especially LDL) in the intima, oxidative modification, recruitment of monocytes/macrophages, foam-cell formation, smooth muscle cell migration/proliferation, extracellular matrix deposition, plaque growth and eventually luminal narrowing and ischemia. [4,8].

In the kidney context, animal models have shown that hypercholesterolaemia exacerbates the renal structural damage when combined with renal artery stenosis: for example, diet-induced hypercholesterolaemia plus renal artery stenosis in pigs or other models led to accelerated fibrosis, impaired perfusion and remodelling compared to stenosis alone. [5,7].

The lipid profile thus may influence not only plaque formation in the renal artery but also downstream intrarenal injury, making lipid spectrum indicators potentially relevant in ARAS beyond just stenosis risk [6].

3.1 Traditional lipid-panel indicators

A community-based cross-sectional study of adults (aged 50-75) undergoing thoraco-abdominal CT angiography found that higher total cholesterol and lower HDL-cholesterol were independently associated with renal artery plaque and stenosis. Specifically, in that Chinese cohort, prevalence of renal artery plaque (RAP) was 28.7 % and atherosclerotic renal artery stenosis (ARAS) was 4.8 %. Older age, hypertension, higher total cholesterol and reduced HDL-cholesterol were associated with RAP and ARAS. ([PubMed][4])

Another study (Karger Publishers, “Lipid Profiles in Patients with Atherosclerotic Renal Artery Stenosis”) compared patients with angiographically proven ARAS and matched controls. They found that while LDL-cholesterol and total cholesterol were numerically higher in the ARAS group (4.06 vs 3.72 mmol/L for LDL, 6.12 vs 5.65 mmol/L for total cholesterol) the differences did not reach statistical significance in their small sample. However, HDL-cholesterol was lower (1.00 vs 1.16 mmol/L) and triglycerides were higher (2.32 vs 1.68 mmol/L). The most pronounced abnormality was lower apolipoprotein A1 in the ARAS group (0.95 vs 2.09 g/L) and lower apoA1/apoB ratio (0.78 vs 1.74) — suggesting that apolipoprotein measurements may offer additional discriminatory value. ([Karger Publishers][5])

Thus, traditional lipid parameters (TC, LDL-C, HDL-C, TG) appear to have association with renal artery atherosclerosis, but the strength of association and independent predictive value remain understudied.

3.2 Apolipoproteins and lipoprotein(a)

The micro-study above (Karger) highlighted that apolipoprotein A1 (apoA1), the main apolipoprotein of HDL, was markedly lower in ARAS patients, and the apoA1/apoB ratio was very low; this implies that measuring apolipoproteins may detect risk better than standard cholesterol measures alone. ([Karger Publishers][5])

More recently, a hospital-based cross-sectional study of 170 hypertensive patients (85 with ARAS and 85 without) in China investigated the role of lipoprotein(a) [Lp(a)] as a potential residual risk factor when LDL-C was well controlled. They found

in a stratified analysis that in the low LDL-C tertile, patients with high Lp(a) concentrations had significantly higher incidence of ARAS (OR 4.77, 95%CI 1.04-21.79, P=0.044). Multivariate adjusted analysis found high Lp(a) independently associated with ARAS (adjusted OR 6.14, 95%CI 1.03-36.47, P=0.046). ([BioMed Central][6])

These findings suggest that in patients whose LDL-C is already low (perhaps via statin treatment or otherwise), Lp(a) may identify residual risk for renal artery atherosclerosis.

3.3 Summary of findings

There is evidence that some lipid spectrum measures are associated with renal artery atherosclerosis (higher total cholesterol, higher LDL-C, lower HDL-C, higher triglycerides) from population and case studies.

Apolipoproteins (especially low apoA1 and low apoA1/apoB ratio) may provide additional discriminatory information in ARAS.

Elevated Lp(a) appears to act as a residual risk factor for ARAS in hypertensive patients with low LDL-C levels.

However, overall, the number of studies is limited, sample sizes small, and there is heterogeneity in measurement, definitions of ARAS, and control for confounding factors.

4. Analytical Considerations for Lipid Spectrum Assessment in ARAS

When evaluating lipid spectrum indicators in patients with suspected or confirmed atherosclerotic renal artery disease, several analytical and practical points merit attention:

1. Definition of ARAS – Studies vary in how ARAS is defined (angiographic ≥50% stenosis, imaging plaque definition, etc.). Standardising the definition facilitates comparison. For example, the Lp(a) study defined ARAS as ≥50% reduction in cross-sectional area on angiography. ([PMC][7])

2. Confounding by systemic atherosclerosis – Many ARAS patients also have coronary or peripheral artery disease, making it challenging to tease out independent associations of lipids with renal-artery involvement.

3. Effect of lipid-lowering therapy – Many patients may be on statins or other lipid-modifying therapies which alter lipid spectrum measures and may affect the association. Stratification by LDL-C levels (as done in the Lp(a) study) helps.

4. Choice of lipid spectrum metrics – Beyond total cholesterol, LDL-C, HDL-C, and TG, additional metrics such as apoA1, apoB, apoA1/apoB ratio, non-HDL cholesterol, Lp(a), remnant cholesterol, atherogenic index (e.g., TG/HDL-C) may offer incremental insight.

5. Analytical thresholds and residual risk – The concept of "residual risk" refers to risk persisting despite target LDL-C. In ARAS patients with low LDL-C, elevated Lp(a) appears to identify increased risk.

6. Kidney function interplay – Renal impairment itself may alter lipid metabolism (e.g., dyslipidaemia in chronic kidney disease) and complicate interpretation of lipid spectrum measures.

7. Prognostic vs diagnostic value – Whether lipid spectrum indicators predict progression of ARAS, renal function decline, or cardiovascular outcomes in ARAS remains to be established.

5. Implications for Clinical Practice and Research

5.1 Clinical implications

In patients with hypertension and suspected renovascular disease, performing a comprehensive lipid spectrum assessment (including apoA1, apoB, Lp(a)) may help identify those at higher risk of renal artery atherosclerosis, especially if LDL-C is already optimised.

Lower apoA1/apoB ratio or elevated Lp(a) may prompt closer imaging and follow-up for ARAS.

Lipid-modifying therapy in ARAS may need to target beyond LDL-C reduction (for example, therapies reducing Lp(a), raising HDL-C/apoA1) though evidence is not yet strong in this specific population.

Monitoring and managing dyslipidaemia remain important in ARAS given its systemic atherosclerosis context.

5.2 Research implications

Larger prospective studies are needed to confirm the independent predictive value of lipid spectrum markers (apoA1, apoB, Lp(a), remnant cholesterol, non-HDL-C, atherogenic index) for ARAS incidence, progression and outcomes.

Standardised definition of ARAS, ideally with imaging protocols and uniform lipid measurement, will enhance comparability.

Interventional studies to test whether modifying these lipid spectrum markers (e.g., Lp(a)-lowering therapies) improves renal and cardiovascular outcomes in ARAS are warranted.

Studies in diverse populations (including non-Asian, women, different age strata) are needed.

Mechanistic research (animal models, histological correlation) to elucidate how lipoprotein profiles influence renal artery atherosclerosis specifically (beyond other vascular beds) will deepen understanding.

6. Proposed Evaluation Framework for Lipid Spectrum in ARAS

Based on current evidence, the following evaluation framework is proposed for patients with suspected or confirmed atherosclerotic renal artery disease:

1. Traditional lipid panel: total cholesterol, LDL-C, HDL-C, triglycerides

2. Non-HDL cholesterol (total cholesterol minus HDL-C)

3. Apolipoproteins: apoA1, apoB, and calculation of apoA1/apoB ratio

4. Lipoprotein(a) [Lp(a)]

5. Atherogenic indices: e.g., TG/HDL-C ratio, non-HDL/HDL ratio

6. Consider remnant cholesterol (total cholesterol – LDL-C – HDL-C) if available

7. Stratify risk: patients with low LDL-C but elevated Lp(a) and/or low apoA1/apoB ratio may be considered higher risk for ARAS

8. Integrate lipid findings with clinical factors (age, hypertension duration, renal function, albuminuria, other atherosclerosis) to guide imaging decisions and therapeutic intensity

Conclusion.

In summary, the lipid spectrum provides important insight into the atherosclerotic process in the renal arteries. Traditional lipid parameters retain relevance, but additional markers such as apolipoprotein A1, apoB, apoA1/apoB ratio and lipoprotein(a) appear to offer incremental value in identifying risk of atherosclerotic renal artery disease. In hypertensive patients with low LDL-C, elevated Lp(a) may represent a significant residual risk for ARAS. Nonetheless, the evidence base is modest and further prospective and interventional research is needed. Clinicians should consider more comprehensive lipid-spectrum assessment in patients at risk for ARAS, integrate results into a broader cardiovascular/renal risk framework, and remain alert to the possibility of renal-artery involvement in patients with dyslipidaemia and renovascular syndromes.

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