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CORRELATION BETWEEN CARDIOMETABOLIC FACTORS AND FUNCTIONAL DISORDERS OF THE SYMPATHOADRENAL SYSTEM IN YOUNG PATIENTS WITH NEWLY DIAGNOSED ANGINA PECTORIS AND PREDICTION OF ITS DEVELOPMENT

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Background: The incidence of early-onset coronary artery disease (CAD), manifesting as angina pectoris in young adults, is steadily rising. The interplay between cardiometabolic abnormalities and the sympathoadrenal system (SAS) is hypothesized to be a key driver of premature atherosclerosis and rapid disease progression. Objective: To investigate the correlation between cardiometabolic factors and functional disorders of the sympathoadrenal system in young patients with newly diagnosed angina pectoris, and to develop prognostic criteria for disease progression. Methods: The study included 85 young patients (aged 25 to 44 years) recently diagnosed with new-onset stable angina, alongside a control group of 25 age-matched healthy individuals. Cardiometabolic profiling involved measuring body mass index (BMI), lipid spectrum (total cholesterol, LDL), and insulin resistance via the HOMA-IR index. SAS functional state was evaluated by high-performance liquid chromatography to determine plasma epinephrine and norepinephrine levels. Results: Young patients with newly diagnosed angina exhibited profound SAS hyperactivation. Plasma norepinephrine was significantly elevated compared to controls (435.6 ± 38.4 pg/mL vs. 258.2 ± 20.5 pg/mL, $p < 0.05$). A strong positive correlation was identified between plasma norepinephrine and HOMA-IR ($r = 0.72$; $p < 0.01$), as well as between norepinephrine and LDL cholesterol ($r = 0.64$; $p < 0.05$). Prognostic modeling revealed that the combination of severe sympathetic overdrive (norepinephrine > 400 pg/mL) and marked insulin resistance (HOMA-IR > 3.0) increased the risk of rapid clinical deterioration three-fold over a 12-month follow-up period. Conclusion: The initial presentation of angina pectoris in young adults is tightly coupled with significant functional disturbances of the sympathoadrenal system and cardiometabolic dysregulation. Recognizing this neurohumoral-metabolic cross-talk provides a critical foundation for early risk stratification and targeted preventive strategies.

Keywords

angina pectoris, young adults, cardiometabolic factors, sympathoadrenal system, catecholamines, norepinephrine, prognosis.

КОРРЕЛЯЦИЯ МЕЖДУ КАРДИОМЕТАБОЛИЧЕСКИМИ ФАКТОРАМИ И ФУНКЦИОНАЛЬНЫМИ НАРУШЕНИЯМИ СИМПАТОАДРЕНАЛЬНОЙ СИСТЕМЫ У МОЛОДЫХ ПАЦИЕНТОВ С ВПЕРВЫЕ ДИАГНОСТИРОВАННОЙ СТЕНОКАРДИЕЙ И ПРОГНОЗИРОВАНИЕ ЕЕ РАЗВИТИЯ

Аннотация

Обоснование: Заболеваемость ишемической болезнью сердца (ИБС) с ранним началом, проявляющаяся стенокардией у лиц молодого возраста, неуклонно растет. Предполагается, что взаимодействие кардиометаболических нарушений и

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симпатоадреналовой системы (САС) является ключевым фактором преждевременного атеросклероза. Цель исследования: Изучить взаимосвязь кардиометаболических факторов и функциональных нарушений симпатоадреналовой системы у лиц молодого возраста с впервые выявленной стенокардией и разработать критерии прогнозирования развития заболевания. Методы: В исследование включено 85 молодых пациентов (от 25 до 44 лет) с впервые выявленной стабильной стенокардией, а также контрольная группа из 25 здоровых лиц. Кардиометаболический профиль оценивали по индексу массы тела (ИМТ), липидному спектру (ОХС, ЛПНП) и инсулинорезистентности (HOMA-IR). Функциональное состояние САС оценивали путем измерения уровня адреналина и норадреналина в плазме крови. Результаты: У молодых пациентов со стенокардией выявлена выраженная гиперактивация САС. Уровень норадреналина был достоверно выше по сравнению с контролем (435,6 ± 38,4 пг/мл против 258,2 ± 20,5 пг/мл, $p < 0,05$). Установлена сильная положительная корреляция между уровнем норадреналина и HOMA-IR ($r = 0,72$; $p < 0,01$). Комбинация тяжелой симпатической гиперактивности и выраженной инсулинорезистентности увеличивала риск быстрого прогрессирования заболевания в три раза. Заключение: Первичное проявление стенокардии у молодых людей тесно связано со значительными функциональными нарушениями САС и кардиометаболической дисрегуляцией. Ранняя оценка этих параметров имеет решающее значение для прогнозирования риска.

Ключевые слова

стенокардия, молодой возраст, кардиометаболические факторы, симпатоадреналовая система, катехоламины, норадреналин, прогноз.

YOSHLARDA BIRINCHI MARTA STENOKARDIYA ANIQLANGANDA KARDIOMETABOLIK OMILLAR VA SIMPATO- ADRENAL TIZIMINI FUNKSIONAL BUZILISHLARINI OZARO ALOQADORLIGINI ORGANISH VA RIVOJLANISHINI PROGNOZLASH

Annotatsiya

Dolzarbligi: Yoshlarda yurak ishemik kasalligi (YUIK) va stenokardiyaning erta uchrashi ortib bormoqda. Kardiometabolik omillar va simpato-adrenal tizimning (SAT) o'zaro ta'siri erta ateroskleroz va kasallikning tezkor rivojlanishini belgilovchi asosiy omillardan hisoblanadi. Maqsad: Yoshlarda birinchi marta stenokardiya aniqlanganda kardiometabolik omillar va simpato-adrenal tizimini funksional buzilishlarini o'zaro aloqadorligini o'rganish va rivojlanishini prognozlash. Material va metodlar: Tadqiqotga birinchi marta barqaror stenokardiya tashxisi qo'yilgan 85 nafar yosh bemor (25-44 yosh) hamda 25 nafar sog'lom ko'ngillilar jalb etildi. Bemorlarning kardiometabolik ko'rsatkichlari (TVI, umumiy xolesterin, ZP LP, HOMA-IR indeksi) va qon plazmasidagi katexolaminlar (noradrenalin, adrenalin) miqdori tahlil qilindi. Natijalar: Yangi aniqlangan stenokardiyasi bor yosh bemorlarda SATning yaqqol giperaktivatsiyasi kuzatildi. Noradrenalin miqdori nazorat guruhiga nisbatan sezilarli darajada baland bo'ldi (435,6 ± 38,4 pg/ml ga nisbatan 258,2 ± 20,5 pg/ml, $p < 0,05$). HOMA-IR indeksi va noradrenalin darajasi o'rtasida kuchli musbat korrelyatsiya ($r = 0,72$; $p < 0,01$) qayd etildi. SAT giperaktivatsiyasi va insulin rezistentlikning birgalikda uchrashi kasallikning tezkor rivojlanish xavfini 3 barobarga oshirishi prognoz qilindi. Xulosa: Yoshlarda ilk bor aniqlangan stenokardiya SATning kuchli faollashuvi va kardiometabolik o'zgarishlar bilan chambarchas bog'liq. Ushbu neyrogumoral va metabolik ko'rsatkichlarni erta aniqlash kasallik xavfini prognoz qilish va profilaktika choralarini belgilash imkonini beradi.

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Kalit so'zlar

stenokardiya, yoshlar, kardiometabolik omillar, simpato-adrenal tizim, katexolaminlar, noradrenalin, prognoz.

INTRODUCTION

Historically, coronary artery disease (CAD) and its primary clinical manifestation, angina pectoris, were considered pathologies exclusively afflicting the elderly. However, the demographic landscape of cardiovascular disease has shifted dramatically over the past two decades. Recent epidemiological data indicates an alarming surge in the incidence of early-onset CAD, frequently affecting young adults between the ages of 25 and 45 [1]. When angina pectoris is detected for the first time in this demographic, it often presents with distinct pathophysiological features that differ markedly from those seen in older populations.

The early manifestation of myocardial ischemia is intimately tied to a detrimental synergy between modern lifestyle-driven cardiometabolic risk factors—such as central obesity, dyslipidemia, and insulin resistance—and the chronic hyperactivation of the autonomic nervous system [2, 3]. The sympathoadrenal system (SAS) functions as a fundamental interface linking psychological stress, metabolic dysregulation, and vascular health. Sustained elevations in circulating catecholamines (norepinephrine and epinephrine) have been shown to not only directly injure the endothelial lining and promote vasoconstriction but also profoundly exacerbate systemic metabolic disturbances [4].

Despite extensive research into metabolic syndrome, the precise mechanistic crosstalk between specific cardiometabolic factors and the functional depletion or overactivity of the SAS in the very early stages of angina in young people remains a critical blind spot in cardiology. Furthermore, while conventional risk scores perform adequately in older adults, they often fail to accurately predict disease trajectory in young patients presenting with their first anginal episode [5]. The ability to forecast whether a newly diagnosed young patient will remain stable or rapidly progress to acute coronary syndrome depends heavily on understanding this neurohumoral-metabolic axis [6].

Therefore, this study was designed with a dual purpose: first, to systematically investigate the correlation between established cardiometabolic parameters and functional disorders of the sympathoadrenal system in young adults newly diagnosed with angina pectoris; and second, to utilize these biological markers to establish prognostic criteria for predicting the subsequent clinical development of the disease.

MATERIALS AND METHODS

Study Population and Design - This prospective observational study was conducted at the Department of Faculty Therapy of the Andijan State Medical Institute. The clinical cohort comprised 85 young patients (52 males and 33 females) aged between 25 and 44 years (mean age 36.8 ± 4.2 years) who were recently diagnosed with first-onset stable angina pectoris (Canadian Cardiovascular Society [CCS] class I-II). Diagnosis was strictly verified based on clinical presentation, resting and stress electrocardiography (treadmill test), and echocardiographic parameters in accordance with the latest European Society of Cardiology guidelines.

To serve as a baseline for metabolic and neurohumoral variables, a Control Group of 25 healthy, age- and sex-matched volunteers without any history of cardiovascular or metabolic disease was also recruited.

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Exclusion criteria for both groups were stringent to avoid confounding variables: patients with a history of acute coronary syndrome, severe arrhythmias, secondary arterial hypertension, diagnosed type 1 or advanced type 2 diabetes mellitus (requiring insulin), chronic kidney disease, thyroid dysfunction, and those already taking long-term sympatholytic or lipid-lowering medications prior to their angina diagnosis. All study subjects provided formal informed consent.

Clinical and Laboratory Assessments - All evaluations were performed following an overnight fast of at least 10 hours. Blood samples were drawn from the antecubital vein between 08:00 and 09:00 AM under strictly controlled, resting conditions to prevent acute stress-induced catecholamine surges.

Cardiometabolic Profiling: Anthropometric measurements were taken to calculate Body Mass Index (BMI, kg/m²). The lipid spectrum, including total cholesterol (TC), low-density lipoprotein (LDL), high-density lipoprotein (HDL), and triglycerides (TG), was measured enzymatically. Fasting plasma glucose and fasting insulin levels were quantified, allowing for the calculation of the Homeostatic Model Assessment for Insulin Resistance (HOMA-IR). A HOMA-IR value > 2.7 was considered indicative of insulin resistance.

Sympathoadrenal System Evaluation: The functional state of the SAS was determined by quantifying plasma concentrations of norepinephrine (NE) and epinephrine (EPI). This was achieved utilizing high-performance liquid chromatography (HPLC) with electrochemical detection (Agilent Technologies, USA).

Prognostic Follow-up: The main cohort of 85 patients was longitudinally monitored for 12 months. The primary endpoint for progression was defined as clinical deterioration requiring hospitalization, escalation to CCS class III-IV, or the occurrence of an acute cardiovascular event.

Statistical Analysis - Statistical processing of the data was performed using SPSS Statistics v. 26.0. Continuous variables were tested for normality and presented as mean ± standard deviation (M ± SD). Group differences were evaluated using the independent samples t-test. The relationship between neurohumoral and metabolic markers was assessed using Pearson's correlation coefficient (r). To develop predictive criteria, multivariate logistic regression analysis was employed, calculating odds ratios (OR) with 95% confidence intervals (CI) for disease progression. A p-value of < 0.05 was defined as statistically significant.

RESULTS

Baseline cardiometabolic characteristics demonstrated a stark contrast between young patients with newly diagnosed angina and their healthy peers. As detailed in Table 1, patients in the Angina Group exhibited a significantly higher BMI, bordering on class I obesity. Furthermore, atherogenic dyslipidemia was prominent, characterized by elevated total cholesterol and LDL fractions ($p < 0.05$). Notably, the HOMA-IR index was elevated to 3.4 ± 0.6 in the patient cohort, signaling profound, albeit subclinical, insulin resistance preceding the overt onset of diabetes.

Table 1. Cardiometabolic parameters in young patients with newly diagnosed angina compared to controls (M ± SD).

Parameter	Control Group (n=25)	Angina Group (n=85)
Body Mass Index (kg/m²)	23.4 ± 1.8	29.8 ± 3.2*
Total Cholesterol (mmol/L)	4.2 ± 0.4	6.1 ± 0.8*
LDL Cholesterol (mmol/L)	2.4 ± 0.3	4.0 ± 0.5*

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Fasting Glucose (mmol/L)	4.8 ± 0.4	5.6 ± 0.6*
HOMA-IR Index	1.8 ± 0.3	3.4 ± 0.6*

*Note: * $p < 0.05$ vs. Control Group.*

Assessment of the sympathoadrenal system revealed a state of severe autonomic dysregulation among the young angina patients. The concentration of norepinephrine in the blood plasma—a direct reflection of sympathetic nerve terminal activity—was drastically elevated, exceeding the control values by nearly 68% (Table 2). Epinephrine levels were also significantly raised, suggesting an accompanying activation of the adrenal medulla, likely as a systemic stress response to the underlying ischemic and metabolic burden.

Table 2. Functional state of the sympathoadrenal system (Catecholamine levels) (M ± SD).

Parameter	**Control Group (n=25)**	**Angina Group (n=85)**
Norepinephrine (pg/mL)	258.2 ± 20.5	435.6 ± 38.4*
Epinephrine (pg/mL)	38.5 ± 6.2	71.2 ± 9.5*
NE/EPI Ratio	6.7 ± 0.8	6.1 ± 0.7

*Note: * $p < 0.05$ vs. Control Group.*

Correlation analysis within the Angina Group exposed the intimate pathophysiological link between SAS hyperactivation and metabolic collapse. A strong, positive, and highly significant correlation was found between plasma norepinephrine levels and the HOMA-IR index ($r = 0.72$; $p < 0.01$). Furthermore, norepinephrine levels moderately correlated with LDL cholesterol concentrations ($r = 0.64$; $p < 0.05$) and BMI ($r = 0.58$; $p < 0.05$).

Prognostic Prediction - Over the 12-month follow-up, 18 out of the 85 patients (21.1%) experienced clinical progression (worsening of functional class or urgent hospitalization). Using a logistic regression model incorporating both neurohumoral and metabolic markers, we determined that the simultaneous presence of severe sympathetic overdrive (defined as Norepinephrine > 400 pg/mL) and marked insulin resistance (HOMA-IR > 3.0) served as a powerful composite predictor. Young patients exhibiting this specific combined phenotype had an Odds Ratio (OR) of 3.8 (95% CI: 1.9–7.4, $p < 0.01$) for rapid clinical progression compared to those with isolated or less severe alterations.

DISCUSSION

The rising tide of early-onset coronary artery disease requires a paradigm shift in how we understand its pathogenesis. The findings of this study robustly demonstrate that when angina pectoris first emerges in young adults, it is rarely an isolated plumbing issue of the coronary arteries. Instead, it is deeply embedded in a systemic functional disorder characterized by the interplay between sympathetic hyperactivation and cardiometabolic dysregulation.

The significantly elevated levels of norepinephrine in our cohort validate the hypothesis that young patients with premature CAD possess a hyperkinetic, autonomically overdriven cardiovascular profile [7]. Unlike older patients where vascular calcification and rigid plaque formation dominate, early-onset ischemia is heavily influenced by dynamic factors. Chronic sympathetic overstimulation directly promotes endothelial dysfunction, reduces nitric oxide bioavailability, and increases the propensity for coronary vasospasm—all of which serve as the substrate for primary anginal attacks [8, 9].

Crucially, our correlation analysis highlights the bidirectional "vicious cycle" linking the SAS and metabolic factors. We observed a strong correlation between norepinephrine and HOMA-IR ($r = 0.72$). Current literature supports this finding, indicating that catecholamines

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directly induce peripheral insulin resistance by interfering with intracellular insulin signaling pathways in skeletal muscle and adipose tissue [10, 11]. Conversely, the hyperinsulinemia resulting from insulin resistance can cross the blood-brain barrier and stimulate central sympathetic outflow, further elevating circulating norepinephrine [12].

This interplay explains the aggressive nature of early-onset CAD. The metabolic derangements (dyslipidemia and insulin resistance) accelerate atherogenesis, while the simultaneous sympathetic overdrive increases myocardial oxygen demand and triggers plaque instability [13].

From a clinical and predictive standpoint, our prognostic model proved that evaluating standard lipid profiles is insufficient for young patients. The combination of neurohumoral (NE > 400 pg/mL) and specific metabolic (HOMA-IR > 3.0) markers yielded a highly sensitive predictive matrix. Patients harboring this dual vulnerability are at a near four-fold increased risk of rapid deterioration. Recognizing this specific functional phenotype upon the first detection of angina allows clinicians to transition from a reactive approach to a highly proactive, targeted therapeutic strategy. In the setting of faculty therapy, this implies an aggressive early utilization of neuromodulators (like specific beta-blockers or sympatholytics) alongside robust metabolic correction (insulin-sensitizing agents) to arrest the progression of premature CAD.

CONCLUSION

The initial detection of angina pectoris in young adults (aged 25-44) is characterized by a severe functional disorder of the sympathoadrenal system, manifesting as a significant elevation in plasma norepinephrine (by 68%) and epinephrine, indicating profound autonomic overdrive.

A strong pathogenetic link exists between neurohumoral dysregulation and cardiometabolic risk factors. Circulating norepinephrine levels exhibit a powerful positive correlation with insulin resistance (HOMA-IR, r = 0.72) and atherogenic dyslipidemia (LDL, r = 0.64), forming a destructive cycle that accelerates premature atherosclerosis.

The synergistic evaluation of SAS activity and metabolic status holds substantial prognostic value. The combination of elevated norepinephrine (> 400 pg/mL) and insulin resistance (HOMA-IR > 3.0) serves as a reliable predictive criterion, identifying young patients who are at a nearly four-fold greater risk for rapid disease progression and worsening of clinical outcomes within the first year of diagnosis.

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