TIBBIYOT
TA'LIMI & INNOVATSIYALARI

- 14.00.00 - Tibbiyot fanlari;
- 14.00.01 - Akusherlik va ginekologiya;
- 14.00.02 - Morfologiya;
- 14.00.03 - Endokrinologiya;
- 14.00.04 - Otorinolaringologiya;
- 14.00.05 - Ichki kasalliklar;
- 14.00.06 - Kardiologiya;
- 14.00.07 - Gigiena;
- 14.00.08 - Oftal'mologiya;
- 14.00.09 - Pediatriya;
- 14.00.10 - Yuqumli kasalliklar;
- 14.00.11 - Dermatologiya va venerologiya;
- 14.00.12 - Tibbiy reabilitologiya;
- 14.00.13 - Nevrologiya;
- 14.00.14 - Onkologiya;
- 14.00.15 - Patologik anatomiya;
- 14.00.16 - Normal va patologik fiziologiya;
- 14.00.17 - Farmakologiya va klinik farmakologiya;
- 14.00.18 - Psixiatriya va narkologiya;
- 14.00.19 - Klinik radiologiya;
- 14.00.20 - Tibbiy genetika;
- 14.00.21 - Stomatologiya;
- 14.00.22 - Travmatologiya va ortopediya;
- 14.00.23 - Hamshiralik ishini tashkil etish;
- 14.00.24 - Sud tibbiyoti;
- 14.00.27 - Xirurgiya;
- 14.00.28 - Neyroxirurgiya;
- 14.00.41 - Xalq tabobati;
- 14.00.35 - Bolalar xirurgiyasi;
- 14.00.34 - Yurak-qon tomir xirurgiyasi

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2026-yil, yanvar

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MUNDARIJA

MORPHOLOGICAL AND MORPHOMETRIC CHANGES IN THE MYOCARDIUM OF THE HEART UNDER CONDITIONS OF EXPERIMENTAL HYPERPARATHYROIDISM

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Abstract: Experimental hyperparathyroidism is accompanied by profound disturbances of mineral metabolism, primarily hypercalcemia and phosphorus imbalance, which adversely affect the structural and functional state of the myocardium. The present study aimed to comprehensively evaluate morphological and morphometric alterations in the heart muscle under conditions of experimental hyperparathyroidism. The experimental model was reproduced in laboratory animals by sustained induction of hyperparathyroid state. Myocardial samples were subjected to histological and morphometric analysis using standard staining techniques with subsequent quantitative assessment of cardiomyocyte diameter, interstitial space, and fibrotic component volume fraction. Morphological examination revealed pronounced dystrophic and vacuolar degeneration of cardiomyocytes, fragmentation and lysis of myofibrils, focal necrobiotic changes, and marked microcirculatory disturbances, including vascular congestion and perivascular edema. Expansion of the interstitial connective tissue and activation of fibroblastic elements were also observed. Morphometric analysis demonstrated a significant increase in cardiomyocyte diameter, thickening of myocardial fibers, and a statistically significant elevation in the relative area of fibrotic components compared to controls ($p < 0.05$).
These findings indicate that mineral metabolism imbalance in hyperparathyroidism induces structural remodeling of the myocardium characterized by hypertrophic and fibrotic changes. Such remodeling forms the morphological substrate for the development of heart failure and cardiac rhythm disturbances. The results expand current understanding of cardiovascular complications associated with hyperparathyroidism and highlight the importance of early pathogenetic correction of mineral imbalance to prevent myocardial damage.

Key words: mineral metabolism; myocardium; cardiomyocytes; fibrosis; myocardial remodeling.

Annotatsiya: Eksperimental giperparatireoz minerallar almashinuvining chuqur buzilishlari, birinchi navbatda, miokardning strukturaviy-funksional holatiga salbiy ta'sir ko'rsatadigan giperkalsiyemiya va fosfor muvozanatining buzilishi bilan birga keladi. Ushbu tadqiqot eksperimental giperparatireoz sharoitida yurak mushaklarining morfologik va morfometrik o'zgarishlarini kompleks baholashga qaratilgan. Eksperimental model laboratoriya hayvonlarida giperparatireoid holatni barqaror induksiya qilish orqali amalga oshirildi. Miokard namunalari standart bo'yash usullaridan foydalangan holda gistologik va morfometrik tahlil qilindi, so'ngra kardiomiotsitlar diametri, interstitsial bo'shliq va fibroz komponentning hajmiy fraksiyasi miqdoriy baholandi. Morfologik tekshiruvda kardiomiotsitlarning yaqqol distrofik va vakuol degeneratsiyasi, miofibrillalarning parchalanishi va lizisi, fokal nekrobiotik o'zgarishlar, mikrotsirkulyatsiyaning yaqqol buzilishi, shu jumladan tomirlar to'laqonligi va perivaskulyar shish aniqlandi. Shuningdek, interstitsial biriktiruvchi to'qimaning kengayishi va fibroblastik elementlarning faollashuvi kuzatildi. Morfometrik tahlil kardiomiotsitlar diametrining sezilarli darajada oshishini, miokard tolalarining qalinlashishini va fibroz komponentlarning nisbiy maydonining nazoratga nisbatan statistik jihatdan sezilarli darajada oshishini ko'rsatdi ($r<0,05$).

Bu ma'lumotlar shundan dalolat beradiki, giperparatireozda minerallar almashinuvi disbalansi gipertrofik va fibroz o'zgarishlar bilan xarakterlanuvchi miokardning strukturaviy o'zgarishini indutsirlaydi. Bunday remodellanish yurak yetishmovchiligi va yurak ritmi buzilishining rivojlanishi uchun morfologik substratni shakllantiradi. Natijalar giperparatireoz bilan bog'liq yurak-qon tomir asoratlari haqidagi zamonaviy tushunchani kengaytiradi va miokard shikastlanishining oldini olish uchun mineral disbalansni erta patogenetik tuzatish muhimligini ta'kidlaydi.

Kalit so'zlar: Eksperimental giperparatireoz; miokard; morfologik o'zgarishlar; morfometriya; yurak remodellasiyasi; fibroz; mineral almashinuv buzilishi; kardiomiositlar; yurak yetishmovchiligi.

Аннотация: Экспериментальный гиперпаратиреоз сопровождается глубокими нарушениями минерального обмена, прежде всего гиперкальциемией и фосфорным дисбалансом, которые отрицательно влияют на структурно-функциональное состояние миокарда. Данное исследование было направлено на комплексную оценку морфологических и морфометрических изменений сердечной мышцы в условиях экспериментального гиперпаратиреоза. Экспериментальная модель воспроизводилась на лабораторных животных путем устойчивой индукции гиперпаратиреоидного состояния. Образцы миокарда были подвергнуты гистологическому и морфометрическому анализу с использованием стандартных методов окрашивания с последующей количественной оценкой диаметра кардиомиоцитов, интерстициального пространства и объемной фракции фиброзного компонента. Морфологическое исследование выявило выраженную дистрофическую и вакуолярную дегенерацию кардиомиоцитов, фрагментацию и лизис миофибрилл, очаговые некробиотические изменения, выраженные нарушения микроциркуляции, включая сосудистое полнокровие и периваскулярный отек. Также наблюдалось расширение интерстициальной соединительной ткани и активация фибробластических элементов. Морфометрический анализ показал достоверное увеличение диаметра кардиомиоцитов, утолщение волокон миокарда и статистически значимое повышение относительной площади фиброзных компонентов по сравнению с контролем ($p < 0,05$).

Эти данные свидетельствуют о том, что дисбаланс минерального обмена при гиперпаратиреозе индуцирует структурное преобразование миокарда, характеризующееся гипертрофическими и фиброзными изменениями. Такое ремоделирование формирует морфологический субстрат для развития сердечной недостаточности и нарушений сердечного ритма. Результаты расширяют современное понимание сердечно-сосудистых осложнений, связанных с гиперпаратиреозом, и подчеркивают важность ранней патогенетической коррекции минерального дисбаланса для предотвращения повреждения миокарда.

Ключевые слова: Экспериментальный гиперпаратиреоз; миокард; морфологические изменения; морфометрия; ремоделирование сердца; фиброз; нарушение минерального обмена; кардиомиоциты; сердечная недостаточность.

INTRODUCTION

Hyperparathyroidism is an endocrine disorder characterized by excessive secretion of parathyroid hormone (PTH), resulting in profound disturbances of calcium–phosphorus homeostasis and systemic metabolic imbalance. [4] Persistent elevation of PTH leads to hypercalcemia, altered intracellular calcium handling, oxidative stress, and mitochondrial dysfunction, all of which adversely affect highly specialized tissues, including the myocardium.[6] While skeletal and renal complications of hyperparathyroidism are well documented, cardiovascular involvement has increasingly been recognized as a major determinant of morbidity and mortality.

Experimental and clinical studies indicate that chronic exposure to elevated PTH levels contributes to myocardial hypertrophy, interstitial fibrosis, microvascular dysfunction, and impaired contractility.[8] Calcium overload within cardiomyocytes disrupts excitation–contraction coupling, promotes myofibrillar disorganization, and activates profibrotic signaling pathways. In addition, mineral metabolism imbalance may enhance collagen deposition and extracellular matrix remodeling, thereby altering myocardial stiffness and electrical conductivity. These structural alterations create a morphological substrate for the development of heart failure and cardiac arrhythmias.[7] Despite growing evidence of cardiovascular complications associated with hyperparathyroidism, the detailed morphological and morphometric characteristics of myocardial remodeling under experimental conditions remain insufficiently elucidated.[3] Quantitative assessment of cardiomyocyte dimensions and fibrotic components is essential for understanding the extent of structural reorganization and its potential functional consequences. Therefore, the present study aimed to investigate the morphological and morphometric changes in the myocardium under conditions of experimental hyperparathyroidism, with particular emphasis on cardiomyocyte remodeling, interstitial fibrosis, and microcirculatory alterations. A comprehensive structural evaluation may contribute to a deeper understanding of the pathogenetic mechanisms underlying cardiac dysfunction in mineral metabolism disorders.

LITERATURE REVIEW

The study was performed on adult laboratory rats (Wistar strain), weighing 180–220 g, maintained under standard vivarium conditions (12-hour light/dark cycle, controlled temperature and humidity, standard diet and water ad libitum). Animals were randomly divided into two groups: a control group and an experimental group with induced hyperparathyroidism. All experimental procedures were conducted in accordance with international guidelines for the care and use of laboratory animals and were approved by the institutional ethics committee. Experimental hyperparathyroidism was induced by prolonged administration of parathyroid hormone (PTH) in

physiologically relevant doses for a defined experimental period, leading to sustained elevation of circulating calcium levels and disturbance of mineral metabolism. The control group received equivalent volumes of physiological saline. The development of hyperparathyroid state was verified by biochemical assessment of serum calcium and phosphorus levels. At the end of the experimental period, animals were euthanized under appropriate anesthesia. The hearts were excised, rinsed in cold isotonic saline, and fixed in 10% neutral buffered formalin. After routine dehydration and paraffin embedding, serial sections (4–5 μm thick) were prepared using a rotary microtome. Histological sections were stained with hematoxylin and eosin for general morphological assessment and Masson's trichrome for evaluation of connective tissue and fibrotic changes. Slides were examined using light microscopy at various magnifications.

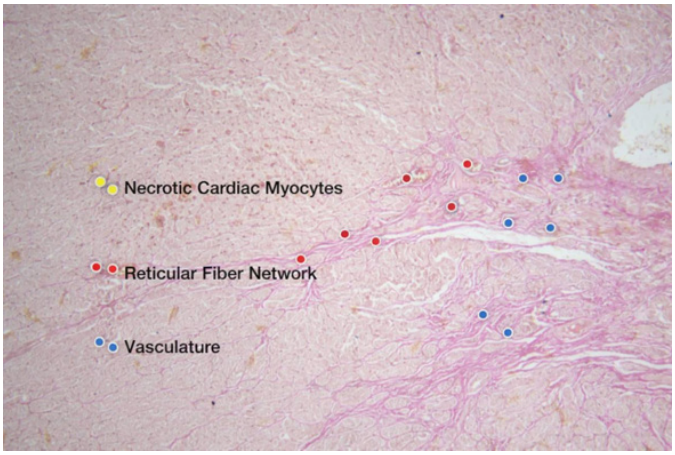

Fig.1. Histological structure of myocardial tissue under experimental conditions.

Hematoxylin and eosin staining. Cardiomyocytes arranged in bundles with eosinophilic cytoplasm and basophilic nuclei; interstitial connective tissue and vascular elements are visible. Scale bar = 100 μm. Morphometric data were analyzed using standard statistical methods. Measurements were obtained from randomly selected microscopic fields in each specimen. Quantitative results are expressed as mean ± standard deviation (mean ± SD).

Qualitative morphological evaluation focused on cardiomyocyte structural integrity, presence of dystrophic and vacuolar changes, myofibrillar organization, vascular alterations, and interstitial remodeling. Morphometric analysis was performed using a digital image analysis system. The following parameters were measured: cardiomyocyte diameter (μm), relative area of interstitial space (%), and volume fraction of fibrotic components (%). Measurements were obtained from multiple randomly selected fields per specimen to ensure representativeness.

Quantitative data were expressed as mean ± standard deviation (M ± SD). Statistical comparisons between groups were performed using appropriate parametric tests after verification of normal distribution. Differences were considered statistically significant at $p < 0.05$. This methodological approach enabled a comprehensive assessment of structural and quantitative myocardial alterations under conditions of experimental hyperparathyroidism.

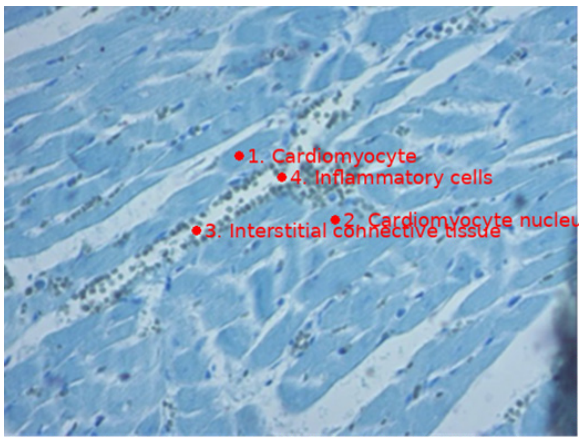

Fig.2. Myocardial tissue under experimental mineral metabolism disorder.

Toluidine blue staining was used for the evaluation of myocardial cellular architecture and interstitial components Toluidine blue staining. Elongated cardiomyocytes with centrally located nuclei; expansion of interstitial connective tissue and accumulation of inflammatory cells are observed. Scale bar = 50 μm.

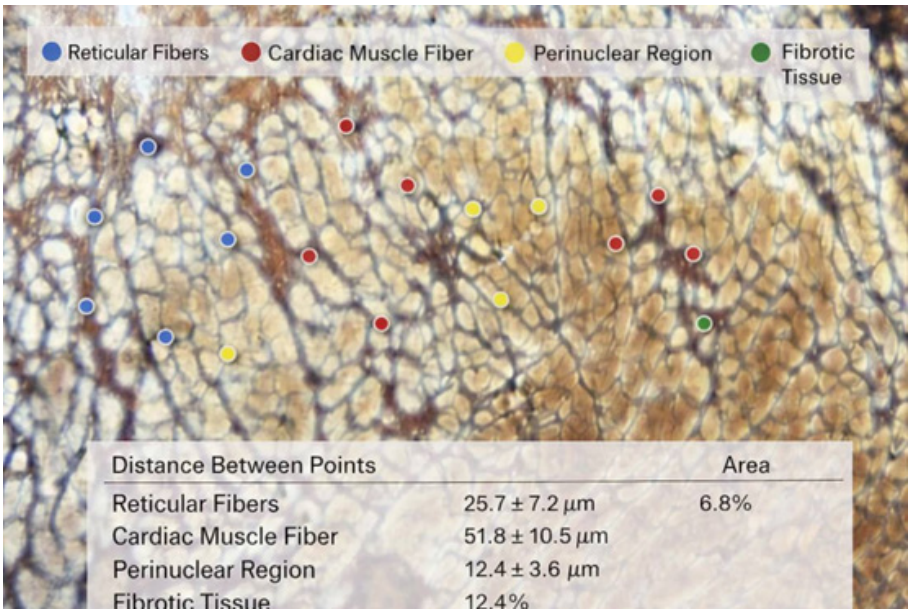

Fig.3. Photomicrograph of Cardiac Tissue Stained with Silver Impregnation Method (Reticulin Stain).

The presented specimen represents myocardial tissue stained with silver impregnation (reticulin stain). Silver staining selectively highlights reticular fibers (type III collagen), which appear as dark brown to black branching networks surrounding cardiomyocytes. Microscopic examination demonstrates: a well-developed reticular fiber network forming a delicate mesh around cardiac muscle fibers. Cardiomyocytes arranged in branching patterns with centrally located nuclei. The reticular framework outlining individual muscle fibers and small vascular structures. Areas of increased fiber density suggestive of interstitial remodeling. Silver impregnation distinctly visualizes the extracellular matrix architecture, particularly the supporting reticulin scaffold of the myocardium.

RESAECH METHODOLOGY

In this article analysis and synthesis, induction and deduction, modelling methods are used

Analysis and Result

Biochemical analysis confirmed the successful induction of experimental hyperparathyroidism, as evidenced by significantly elevated serum calcium levels and altered phosphorus concentrations in the experimental group compared with controls ($p < 0.05$). These findings verified the presence of sustained mineral metabolism imbalance during the study period.

Histological examination of myocardial sections from control animals demonstrated preserved structure of cardiac muscle fibers, orderly arrangement of cardiomyocytes with centrally located nuclei, intact cross-striation, and minimal interstitial connective tissue. Microvascular structures exhibited normal lumen diameter and moderate blood filling. In contrast, the myocardium of animals with experimental hyperparathyroidism showed pronounced structural alterations. Cardiomyocytes exhibited dystrophic and vacuolar degeneration, cytoplasmic rarefaction, and focal loss of cross-striation. In several areas, fragmentation and partial lysis of myofibrils were observed. Nuclear changes included chromatin condensation and occasional pyknosis, indicating early degenerative processes. Marked microcirculatory disturbances were identified, including capillary dilation, vascular congestion, perivascular edema, and endothelial swelling. These alterations were accompanied by expansion of the interstitial space and activation of fibroblastic elements. Masson's trichrome staining revealed a substantial increase in collagen deposition, particularly in perivascular and interstitial regions, indicating progressive fibrotic remodeling. Morphometric analysis demonstrated a statistically significant increase in cardiomyocyte diameter in the experimental group compared with controls ($p < 0.05$), consistent with hypertrophic remodeling. Additionally, the relative area of interstitial connective tissue and the volume fraction of fibrotic components were significantly elevated ($p < 0.05$). The interstitial expansion correlated with the severity of microvascular and degenerative changes (Table1).

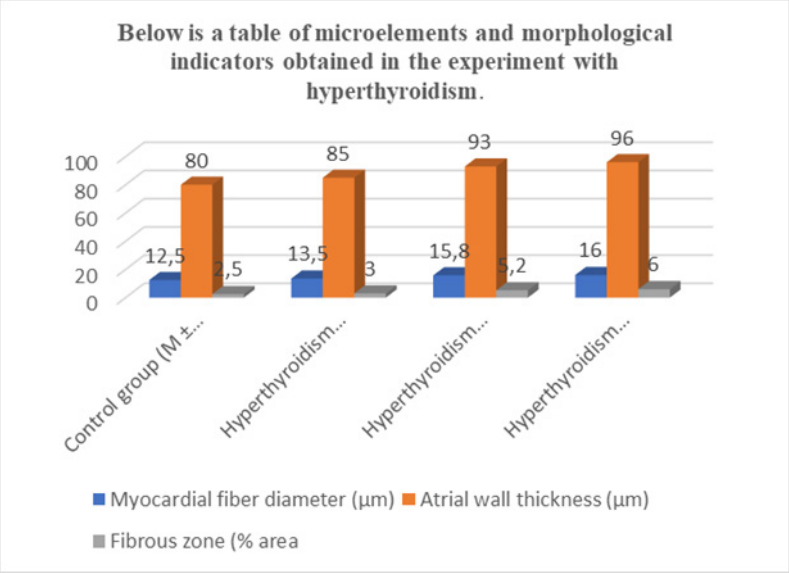

Table1. Morphological parameters of the myocardium in control and hyperthyroid groups.The table presents myocardial fiber diameter (µm), atrial wall thickness (µm), and fibrous zone area (% area). Values are expressed as mean ± standard deviation (SD). Table1 presents the myocardial fiber diameter (µm), atrial wall thickness (µm), and fibrous zone area (% area) in the control group and in Experimental I and II groups, with values expressed as mean ± standard deviation (SD); asterisks indicate statistically significant differences compared with the control group ($p < 0.05$, $p < 0.01$). Overall, the obtained results indicate that experimental hyperparathyroidism induces a complex pattern of myocardial remodeling characterized by cardiomyocyte hypertrophy, degenerative alterations, microvascular dysfunction, and interstitial fibrosis. These structural changes collectively form the morphological basis for impaired myocardial contractility and increased susceptibility to cardiac rhythm disturbances.

The present study demonstrates that experimental hyperparathyroidism induces pronounced structural and morphometric remodeling of the myocardium, characterized by cardiomyocyte hypertrophy, degenerative alterations, microvascular dysfunction, and interstitial fibrosis. These findings expand current evidence that mineral metabolism imbalance plays a pivotal role in cardiovascular pathology. Chronic elevation of parathyroid hormone (PTH) is known to disrupt intracellular calcium homeostasis. Sustained calcium overload in cardiomyocytes impairs excitation–contraction coupling, activates calcium-dependent proteases, and promotes mitochondrial dysfunction. These mechanisms may explain the observed myofibrillar fragmentation, vacuolar degeneration, and cytoplasmic rarefaction. Similar structural alterations have been described in experimental and clinical studies of hypercalcemic states, supporting the concept of calcium-mediated cardiotoxicity. The significant increase in cardiomyocyte diameter observed in this study reflects hypertrophic remodeling. PTH has been reported to stimulate hypertrophic signaling pathways through activation of protein kinase C, mitogen-activated protein kinases (MAPKs), and transforming growth factor-β (TGF-β). Such molecular activation enhances protein synthesis and contributes to myocardial thickening. However, prolonged hypertrophy often progresses to maladaptive remodeling, characterized by stiffness and impaired diastolic function. Interstitial and perivascular fibrosis detected by Masson's trichrome staining indicates activation of fibroblasts and excessive extracellular matrix deposition. Fibrotic remodeling alters myocardial compliance and electrical conduction properties, thereby creating an anatomical substrate for heart failure and rhythmogenesis.

CONCLUSION AND SUGGESTIONS

The expansion of connective tissue and microvascular disturbances observed in the present work are consistent with previously reported associations between hyperparathyroidism and increased cardiovascular morbidity. Microcirculatory abnormalities, including vascular congestion and endothelial swelling, further aggravate tissue hypoxia and oxidative stress. Endothelial dysfunction is increasingly recognized as a key mediator linking mineral metabolism disorders with cardiovascular complications. The combined effects of calcium imbalance, oxidative injury, and profibrotic signaling likely underlie the complex myocardial remodeling identified in this experimental model. Overall, the data confirm that hyperparathyroidism induces structural reorganization of the myocardium that may precede clinically overt cardiac dysfunction. Early correction of mineral metabolism disturbances may therefore represent an important strategy for preventing progressive myocardial damage.

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