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SARCOMERE. THE STRUCTURAL UNIT OF THE MYOFIBRILLAR COMPLEX OF TYPICAL CARDIOMYOCYTES. ISOMETRIC ASPECTS OF SARCOMERE ORGANIZATION

Kobeza P.A. ✉ **Sarcomere. The structural unit of the myofibrillar complex of typical cardiomyocytes. Isometric aspects of sarcomere organization.**
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ABSTRACT. Background. The complexity of understanding the structure and function of cardiomyocytes in the myocardium is a fundamental problem in the field of heart morphology. Sarcomeres are the main structural and functional units of myofibrils. Understanding the organization and dynamics of sarcomeres in cardiomyocytes is crucial for establishing the mechanisms responsible for the process of forming the contractile system of cardiomyocytes. **Objective.** The main purpose of this study is a review of literary sources that complement and expand the essential findings about the construction of myofibrils and their components when studied by effective methods of microscopic techniques. **Materials.** Literature review databases, systematic search of primary sources related to the research topic. Methods of visual examination of the components of sarcomeres and elements of their organization. **Results.** Transmission electron microscopy provides high-resolution imaging of sarcomeres, which is necessary for detailed analysis of their ultrastructure, including visualization of sarcomere components such as Z-discs, M-lines, thick and thin filaments. Morphometric methods are crucial for studying the compaction and orientation of myofibrils in cardiomyocytes. **Conclusion.** Morphometric methods provide valuable information about the structural remodeling of myofibrils in response to physiological stimuli or pathological conditions. These techniques are needed to improve our understanding of the mechanisms underlying muscle contraction and to develop methods to study cardiac remodeling processes in response to the adaptive response.
Key words: sarcomere, actin and myosin, contraction, cardiomyocyte, electron microscopy.

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Background

The complex structure and function of cardiomyocytes in the myocardium have long been of interest to histologists and researchers in the field of cardiac morphology [1]. Sarcomeres, the main structural and functional units of myofibrils, are among the fundamental units contributing to the contractile properties of heart muscle [2]. Understanding the organization and dynamics of sarcomeres in cardiomyocytes is critical to elucidating the morphological subtleties underlying cardiac function and dysfunction [3]. **Objective.** The main goal of this study is to investigate and elucidate the organization, composition and functional significance of sarcomeres in myofibrils of cardiomyocytes in cardiac muscle. Through comprehensive histological analysis and advanced imaging techniques, we aim to provide a detailed understanding of the spatial arrangement, molecular components, and dynamic properties of sarcomeres in the context of cardiac morphology. **Relevance of the study.** The

importance of this study lies in its contribution to fundamental knowledge of cardiac histology and morphology [4]. By revealing the structural complexities of sarcomeres in cardiomyocytes, our study aims to provide insight into the mechanisms underlying cardiac contraction and relaxation [5]. Such insight is essential for advancing our understanding of cardiac physiology and pathophysiology, paving the way for future research efforts to unravel the complex interplay between morphological changes and functional changes in cardiac muscle.

Materials and methods

Literature Review Databases: Researchers often utilize specialized literature review databases such as PubMed, Scopus, Web of Science, or Google Scholar to search for relevant scientific articles, reviews, and meta-analyses. These databases allow for advanced search functionalities, including keyword searches, filters based on publication date and journal, and citation tracking. Systematic Searching: Systematic searching involves following a structured approach to identify relevant literature on a specific topic. This method typically includes defining search terms and criteria, conducting searches across multiple databases, screening search results based on predetermined inclusion and exclusion criteria, and critically appraising selected studies for inclusion in the review. Hand-searching: Hand-searching involves manually searching through the reference lists of relevant articles, reviews, and textbooks to identify additional sources that may not have been captured through electronic databases. This method helps to uncover older or less widely indexed literature and can provide valuable supplementary information for the review.

The Results and discussion

The sarcomere is the basic unit of contraction in striated muscle, including both cardiac and skeletal muscle [6]. It is characterized by a highly organized structure consisting of overlapping thin and thick filaments, as well as specific protein complexes that regulate contraction [7]. Although the basic morphology of sarcomeres in cardiac and skeletal muscle is similar [8], there are important differences that reflect their distinct functions and physiological properties [9]. The morphological structure of the sarcomere includes the localization of basic elements: Z-discs (or Z-lines) are dense protein bands that bisect the sarcomere and anchor thin filaments. They are composed of proteins such as α-actinin and connect adjacent sarcomeres, providing structural stability and facilitating force transmission during contraction. Thin filaments consist mainly of actin, as well as regulatory proteins such as tropomyosin and troponin. These filaments extend inward from the Z-discs and mix with the thick filaments. Thick filaments are composed mainly of myosin, which is responsible for generating force during muscle contraction. Myosin molecules arranged in a checkerboard pattern, with their heads (containing ATPase activity) protruding outwards towards thin filaments. The M-line is a protein structure located in the center of the sarcomere where adjacent thick filaments are attached. It provides structural support and helps maintain the alignment of thick strands during shortening. Titin is a large elastic protein that extends from the Z-disc to the M-line, running along a thick filament. It ensures the elasticity of the sarcomere and contributes to its passive mechanical properties [10]. Sarcomere length: Sarcomere length can vary depending on muscle type and physiological conditions [11]. In skeletal muscle, sarcomeres are typically longer (~2.0-2.4 μm) compared to cardiac muscle sarcomeres (~1.6-2.2 μm).

Differences between the sarcomeres of cardiac and skeletal muscles preserved in the ultrastructural organization. While the sarcomeres of both cardiac and skeletal muscle exhibit striation due to the arrangement of thin and thick filaments, the pattern of striation may be more regular in skeletal muscle, reflecting its highly organized structure and precise arrangement of sarcomeres [12]. Cardiac muscle sarcomeres are connected end-to-end by special junctions called intercalated discs, which contain gap junctions and desmosomes. These structures provide rapid electrical conduction and mechanical coupling between cardiomyocytes, facilitating coordinated cardiac contraction. Cardiomyocytes have a higher density of mitochondria compared to skeletal muscle fibers, reflecting the high energy demand of the heart [13]. This difference in mitochondrial density can affect the distribution and organization of sarcomeres in the cell. Structural differences between cardiac and skeletal muscle sarcomeres reflect their distinct functions. Cardiac muscle sarcomeres are adapted for rhythmic and coordinated contraction to pump blood, whereas skeletal muscle sarcomeres are optimized for voluntary movements and force generation. Formula for the structure of a sarcomere: Sarcomere Length (SL) = 1/2 Length of A-band + Length of I-band. Sarcomere Length (SL): This is the distance between two adjacent Z-lines. By measuring the sarcomere length, we can assess how the length changes during muscle contraction, which is crucial for studying its function. Length of A-band: This is the distance between adjacent M-lines, determined by the length of the thick myosin filaments. The length of the A-band remains constant during muscle contraction, indicating that the thick filaments remain unchanged in length. Length of I-band: This is the distance between adjacent A-bands, determined by the length of the thin actin filaments. The length of the I-band changes during muscle contraction as the thin filaments move toward the center of the sarcomere [14, 15]. These parameters help us understand the structural features of the sarcomere and its role in the process of muscle contraction [16].

Methods of visual examination of sarcomere components and elements of their organization [17]. Electron microscopy (EM): Transmission electron

microscopy (TEM) and scanning electron microscopy (SEM) provide high-resolution images of sarcomeres, which are necessary for detailed analysis of their ultrastructure. TEM, in particular, allows visualization of sarcomere components such as Z-discs, M-lines, thick and thin filaments [18]. Immunofluorescence staining: Immunofluorescence staining combined with fluorescence microscopy is critical for visualizing the spatial distribution and organization of sarcomeres in cardiomyocytes. This method allows the localization of specific sarcomere proteins such as actin, myosin, troponin and titin, providing insight into their location and interactions [19]. Confocal microscopy: Confocal microscopy provides improved optical sectioning and resolution compared to conventional fluorescence microscopy, enabling three-dimensional visualization of sarcomeres. This method is indispensable for studying the spatial organization of sarcomeres in the complex three-dimensional architecture of cardiomyocytes [20]. Fluorescence Resonance Energy Transfer (FRET): FRET is valuable for studying proximity and interactions between sarcomeric proteins, providing insight into their structural organization and dynamics. By measuring the transfer of energy between fluorophores attached to specific proteins, FRET can elucidate molecular interactions within sarcomeres [21]. X-ray diffraction: X-ray diffraction provides information about the molecular arrangement of sarcomere proteins in myofibrils. This technique is important for studying the structural organization of sarcomeres at the atomic level, including the orientation and distance between thick and thin filaments [22]. Atomic force microscopy (AFM): AFM enables high-resolution nanoscale imaging of sarcomeres, providing insight into their mechanical properties and organization. AFM is particularly useful for studying the topography and elasticity of sarcomeres in situ, which contributes to our understanding of cardiac muscle biomechanics [23]. Electronic tomography. Electron tomography makes it possible to reconstruct three-dimensional images of sarcomeres, offering a detailed view of their structural organization and connections with other cellular components [24]. This method is necessary to study the organization of sarcomeres in the complex architecture of cardiomyocytes. Western blotting: Western blotting is valuable for analyzing the expression levels of sarcomere proteins, providing insight into their abundance and potential changes in disease states [25]. This method is indispensable for studying changes in the composition of sarcomeres associated with cardiac pathologies. Cryo-electron microscopy (Cryo-EM): Cryo-EM allows examination of sarcomeres in their native state without the need for chemical fixation, preserving their structural integrity [26]. This method is necessary for studying dynamic processes in sarcomeres and for recording temporal interactions between sarcomere proteins.

Protein-protein interaction studies: Techniques such as co-immunoprecipitation and yeast two-hybrid assays are invaluable for studying interactions between sarcomere proteins [27]. These techniques provide insight into the complex network of protein-protein interactions that govern the assembly, organization, and function of sarcomeres. Morphometric methods play a crucial role in the study of myofibril shortening in cardiac myocytes (cardiomyocytes) [28]. These methods, which involve the quantitative analysis of cellular structures and dimensions, are indispensable for understanding the mechanisms underlying muscle contraction and understanding the morphological changes associated with various physiological and pathological conditions. An important requirement for the use of morphometric methods in the study of myofibril contraction is the accurate measurement of sarcomere parameters. Sarcomeres are the basic contractile units of muscle, consisting of overlapping thin (actin) and thick (myosin) filaments. The length, width and location of sarcomeres directly affect the contractile properties of muscle fibers. Morphometric techniques such as transmission electron microscopy (TEM) and immunofluorescence staining combined with confocal microscopy allow precise measurements of sarcomere length, Z-line spacing, and filament density. These quantitative measurements are important for assessing the structural integrity of sarcomeres and understanding how changes in sarcomere morphology affect muscle function [29].

The molecular mechanism of muscle contraction and relaxation involves the interaction between actin and myosin filaments within the sarcomeres of muscle fibers. This process, known as the sliding filament theory, describes how actin and myosin filaments slide past each other, leading to muscle contraction, and how they disengage to allow for muscle relaxation. Upon muscle stimulation, calcium ions are released from the sarcoplasmic reticulum into the cytoplasm of the muscle cell. Calcium ions bind to the regulatory protein troponin, causing it to change shape and move tropomyosin away from the myosin-binding sites on the actin filaments. With the binding sites exposed, myosin heads (cross-bridges) on the thick filaments bind to specific binding sites on the actin filaments, forming cross-bridges [30].

Energy stored in the myosin heads is released, causing them to change shape and exert force on the actin filaments. This results in the sliding of the actin filaments over the myosin filaments towards the center of the sarcomere, shortening the sarcomere and generating muscle contraction. After the power stroke, ATP binds to the myosin heads, causing them to detach from the actin filaments. The ATP is then hydrolyzed to ADP and inorganic phosphate, providing energy for the next cycle of cross-bridge formation and power stroke. When the muscle is no longer stimulated, calcium ions are actively transported back into the sarcoplasmic reticulum, reducing the calcium ion concentration in the cytoplasm. With the decrease in calcium ion concentration, troponin returns to its original shape, allowing tropomyosin to

once again cover the myosin-binding sites on the actin filaments, preventing cross-bridge formation. Any remaining cross-bridges detach from the actin filaments, and the myosin heads return to their resting conformation. Without the formation of new cross-bridges, the sarcomeres passively return to their resting length due to the elasticity of the titin filaments and other structural proteins [31]. The molecular mechanism of actin-myosin interaction during muscle contraction and relaxation involves a series of highly coordinated steps, including cross-bridge formation, power stroke generation, ATP hydrolysis, and detachment of myosin heads [32]. This intricate process ensures precise control of muscle contraction and relaxation in response to physiological stimuli. Morphometric methods are crucial for studying the compaction and orientation of myofibrils in cardiomyocytes. Cardiac muscle fibers characterized by a highly organized arrangement of myofibrils that align in register to optimize force transmission during contraction. Morphometric techniques, such as image analysis software and 3D reconstruction, allow researchers to quantify the density, orientation, and distribution of myofibrils in cardiomyocytes [33]. By analyzing these morphometric parameters, researchers can assess the degree of compaction and alignment of myofibrils that are necessary for efficient force generation and contraction of the heart muscle.

Conclusion

1. Morphometric methods provide valuable information about the structural remodeling of myofibrils in response to physiological stimuli or pathological conditions. For example, during cardiac hypertrophy or heart failure, myofibrils undergo structural changes, including changes in size, shape, and organization. Morphometric analysis allows us to quantify these structural changes, providing valuable information about the remodeling process and its impact on cardiac function. In addition, morphometry methods can used to evaluate the effectiveness of therapeutic interventions aimed at modulating the structure and function of myofibrils in modeling pathomorphological conditions and studying adaptive reactions of cardiac muscle.

2. The necessity of using morphometry methods in the study of myofibril contraction of cardiac myocytes is due to their ability to provide quantitative data on sarcomere parameters, to evaluate the compaction and orientation of myofibrils, as well as to evaluate structural remodeling in response to physiological and pathological stimuli. These techniques needed to improve our understanding of the mechanisms underlying muscle contraction and to develop methods to study cardiac muscle remodeling processes in response to adaptive responses.

Information on conflict of interest

There are no potential or apparent conflicts of interest related to this manuscript at the time of publication and not anticipated.

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Кобеза П.А. Саркомер. Структурна одиниця міофібрилярного комплексу типових кардіоміоцитів. Аспекти ізометризації в організації саркомера.

РЕФЕРАТ. Актуальність. Складність розуміння структури і функції кардіоміоцитів у міокарді є фундаментальною проблематикою у галузі морфології серця. Саркомери основні структурні та функціональні одиниці міофібрил. Розуміння організації та динаміки саркомерів у кардіоміоцитах має вирішальне значення для встановлення механізмів, що є відповідальними за процес формування скоротливої системи кардіоміоцитів. **Мета.** Основною метою цього дослідження є огляд літературних джерел, які доповнять і розширять істотне уявлення про будову міофібрил і їх компонентів при дослідженні різними методами мікроскопічної техніки. **Матеріал.** Бази даних огляду літератури, систематичний пошук першоджерел пов'язаних із тематикою дослідження. Методи візуального дослідження компонентів саркомерів та елементів їх організації. **Результати.** Трансмісійна електронна мікроскопія забезпечує зображення саркомерів з високою роздільною здатністю, які необхідні для детального аналізу їх ультраструктури, зокрема дозволяє візуалізувати такі компоненти саркомерів, як Z-диски, М-лінії, товсті та тонкі філаменти. Морфометричні методи мають вирішальне значення для вивчення ущільнення та орієнтації міофібрил у кардіоміоцитах. **Підсумок.** Морфометричні методи дають цінну інформацію про структурне ремоделювання міофібрил у відповідь на фізіологічні стимули або патологічні стани. Ці методи необхідні для покращення нашого розуміння механізмів, що лежать в основі скорочення м'язів, і для розробки методів вивчення процесів ремоделювання серцевого м'яза у відповідь на адаптаційну реакцію.

Ключові слова: саркомер, актин і міозин, скорочення, кардіоміоцит, електронна мікроскопія.