

ANNOTATION

of the dissertation by Bauyrzhan Bakhytovich Kaliyev on the topic:
«Оптимизация методов компьютерной и магнитно-резонансной томографии в диагностике патологии левого предсердия у больных с нарушениями ритма сердца» submitted for the degree of Doctor of Philosophy (PhD) in the specialty 8D10102 – «Medicine».

Relevance of the Issue.

Atrial fibrillation (AF) is the most common form of cardiac arrhythmia and is a leading cause of increasing disability and mortality among the population (DiBiase L, Natale A, Romero J. Thrombogenic and arrhythmogenic roles of the left atrial appendage in atrial fibrillation. *Circulation*, 2018).

AF accounts for 60% of all cardioembolic strokes. Cardioembolic sources, primarily atrial thrombi, with most localized in the left atrial appendage (LAA), are the most common sources of (Fuster V, Rydén LE, Cannom DS, et al., 2006).

Approximately 90% of all thrombi are located in the left atrial appendage (LA) (Kong B, Liu Y, Huang H, Jiang H, Huang C. Left atrial appendage closure for thromboembolism prevention in patients with atrial fibrillation: advances and perspectives. *J Thorac Dis*. 2015). Current treatment strategies for AF include both pharmacological and non-pharmacological methods. Most AF patients are treated with antiarrhythmic drugs and anticoagulants, while only those with persistent AF require cardioversion in various forms. Radiofrequency isolation of the pulmonary vein antrum is one of the effective approaches in treating patients with persistent AF. However, the presence of thrombi in the LA appendage is a contraindication to cardioversion. After the normalization of sinus rhythm, restoration of contractile function and blood flow can lead to thrombus dislodgement from the LAA, resulting in cardioembolic stroke.

The “gold standard” for diagnosing thrombi in the LAA is transesophageal echocardiography (TEE) (Sallach JA, Puwanant S, Drinko JK, et al. Comprehensive left atrial appendage optimization of thrombus using surface echocardiography: the CLOTS multicenter pilot trial. *J Am Soc Echocardiogr*, 2009). However, TEE is a semi-invasive procedure that carries a risk of complications. In patients with various esophageal disorders, the risk of wall damage and bleeding increases. In some cases, sedation and anesthetic support are required. It should be noted that TEE does not always rule out LAA thrombosis due to pronounced spontaneous echo contrast, the presence of artifacts, or poor tolerance of the procedure. In this regard, implementing a reliable, non-invasive method for LAA evaluation in clinical practice is essential. Computed tomographic angiography (CTA) is widely used in clinical practice.

Recent advancements in cardiac CTA technology have made this method more appealing due to its non-invasive nature, offering a viable alternative to TEE. Developing risk criteria for thrombosis based on CT imaging could be an effective method in the prevention of thromboembolism. Magnetic resonance imaging (MRI), with its high-resolution capabilities, offers high diagnostic accuracy in detecting LAA thrombosis. This method is non-invasive, safe, and does not require iodine-based contrast agents. For certain patients with a history of iodine allergies, elevated creatinine levels, low glomerular filtration rate, or a low pain threshold, MRI can serve as an alternative diagnostic method for LAA thrombosis, allowing for a morphofunctional assessment of all cardiac structures.

Research Objective:

To improve CT and MRI methods for diagnosing left atrial appendage (LAA) thrombosis in patients with cardiac rhythm disorders.

Research Tasks:

1. To enhance CT and MRI diagnostic methods for identifying left atrial pathology in patients with cardiac rhythm disorders.

2. To conduct a multifactorial analysis in patients with LAA thrombosis.
3. To perform a comparative analysis of CT angiocardiology results with transesophageal echocardiography data.
4. To study gender differences in patients with atrial fibrillation based on echocardiography and computed tomography data.
5. To study anatomical characteristics of the LAA in patients with cardiac rhythm disorders.
6. To develop an optimal diagnostic algorithm for left atrial pathology in patients with cardiac rhythm disorders.

Research Methods:

Collection of patient history and atrial fibrillation risk factors

- Coagulogram
- Cardiac computed tomographic angiography
- Cardiac magnetic resonance imaging
- Transthoracic echocardiography
- Transesophageal echocardiography
- Statistical methods for data analysis
- Collection of patient history and

Research Subjects:

This study investigated groups of patients, comprising 337 individuals with cardiac rhythm disorders and cardiovascular disease risk factors, who underwent examination and treatment at the JSC “National Scientific Cardiac Surgery Center” from 2012 to 2023.

Scientific Contribution

This study introduces several innovations to clinical practice, including:

1. Implementing CT angiocardiology for diagnosing left atrial appendage (LAA) thrombosis in patients with arrhythmias, specifically using a left lateral positioning approach;
2. Using MRI to diagnose LAA thrombosis with detailed assessment of heart chamber function in patients with atrial fibrillation;
3. Providing comparative insights between transesophageal echocardiography and CT for LAA thrombosis diagnosis;
4. Examining the unique morphological characteristics of the LAA;
5. Evaluating gender-related differences in patients with atrial fibrillation.
6. An algorithm for diagnosing left atrial pathology in patients with heart rhythm disorders has been developed.

Practical Significance of the Study

The findings from this study have been implemented in healthcare practice:

1. The diagnostic algorithm for patients with cardiac rhythm disorders is currently in use at the JSC “National Scientific Cardiac Surgery Center.”
2. This methodology is also utilized in medical education, including in universities and in advanced training programs for physicians

Theoretical Significance of the Study

The theoretical significance lies in the potential of the study’s findings to advance the scientific foundation for effective diagnosis and treatment of patients with cardiac rhythm disorders, paving the way for future research in this area.

Key points for defense

1. Positioning patients on their left side during CT angiocardiology of the left atrial appendage improves its filling, thereby eliminating the need for additional targeted scanning and reducing radiation exposure.

2. The “cauliflower” morphological shape of the left atrial appendage increases the risk of thrombus formation and the likelihood of thromboembolic events.

3. CT angiocardiology is a less invasive alternative to transesophageal echocardiography for diagnosing left atrial appendage thrombosis, offering a more refined diagnostic approach for evaluating left heart abnormalities and making it a recommended option for managing patients with rhythm disorders.

4. Cardiac MRI, as a non-invasive and safe diagnostic method, allows assessment of biventricular function while reducing radiation exposure for patients.

Key Presentations of the Dissertation Findings

The main findings of this dissertation were presented at the following conferences:

– The 62nd International Scientific and Practical Conference for Students and Young Scientists, JSC “MUA” (Nur-Sultan, 2020);

– The 9th Eurasian Radiology Forum (Nur-Sultan, 2021);

– The Heart Center’s 10th Anniversary Conference: “Building on Experience, Striving for New Goals” (Nur-Sultan, 2021);

– The 63rd International Scientific and Practical Conference for Students and Young Scientists, JSC “MUA” (Nur-Sultan, 2021);

– The 64th International Scientific and Practical Conference for Students and Young Scientists, JSC “MUA” (Nur-Sultan, 2022);

– The 10th Eurasian Congress of Cardiologists, held online (Moscow, 2022);

– The International Scientific and Practical Conference dedicated to the 85th anniversary of Professor Zhangali Hamzabayevich Khamzabayev (Astana, 2022);

– The 10th Eurasian Radiology Forum (Astana, 2023);

– The Republican Scientific and Practical Conference with International Participation “Modern Trends in Aggressive Cardiology” (Astana, 2023);

– The 65th International Scientific and Practical Conference for Students and Young Scientists, JSC “MUA” (Astana, 2023).

Implementation of Research Results

A computed tomography method for diagnosing left atrial appendage thrombosis in the left lateral position was developed and implemented at the JSC ‘National Scientific Cardiac Surgery Center,’ along with a diagnostic algorithm for suspected cases in patients with cardiac rhythm disorders.

Publications Related to the Dissertation

Four publications were released based on the dissertation research, including three articles in journals recommended by the Committee for Control in the Sphere of Education and Science of the

Ministry of Education and Science of the Republic of Kazakhstan, and one article in a peer-reviewed international journal indexed in the Scopus database (ISSN: 0022-9040, Site Score 1.5, 33rd percentile in the field of medicine).

Conclusions

1. Methods for diagnosing left atrial appendage thrombosis in patients with atrial fibrillation using computed tomography angiography (CTA) and magnetic resonance imaging (MRI) have been developed and optimized, which allows for increased accuracy in detecting thrombi and minimizing the risks associated with invasive procedures.

2. Key risk factors for thrombus formation were identified, including old age, arterial hypertension and diabetes mellitus, which confirms the need to take them into account when planning anticoagulant therapy. The presence of LAA thrombus was significantly associated with diabetes mellitus (OR: 2.12; 44.6, $p=0.003$). An increase in BMI by 1 kg/m² increased the risk of developing left atrial appendage thrombosis by 14% ($p<0.001$). An increase in indexed left ventricular volume by 1 ml/m² increased the likelihood of thrombus formation by 19%. Higher HAS-BLED score was significantly associated with left atrial appendage thrombosis (OR=1.31, $p=0.046$).

3. CTA has demonstrated high sensitivity (97.9%) and diagnostic accuracy, which makes it a reliable alternative to transesophageal echocardiography (TEE), especially for patients with contraindications to invasive methods. The CTA study with the patient lying on the left side showed high diagnostic efficiency, the positive and negative values were 100%.

4. Gender differences in the development of thromboembolic complications were found: women often have a more complex morphology of the auricle and an increased risk of thrombus formation, which requires the use of gender-oriented approaches in diagnosis and treatment. Analysis of comorbidities showed that in males with coronary atherosclerosis, the risk of thrombus formation was increased by 152% (odds ratio = 2.52, $p = 0.001$). An increase in the end-diastolic dimension by 1 cm in women increases the risk of LAA thrombosis by 151% (odds ratio = 2.51, $p = 0.031$). An increase in the end-systolic and end-diastolic volumes of the ventricles by 1 ml in women increases the risk of LAA thrombosis by 4 and 3%, respectively ($p<0.05$). An increase in the indexed end-systolic and end-diastolic volumes of the left ventricle by 1 ml/m² in women increases the risk of LAA thrombosis by 6 and 5%, respectively ($p<0.05$). An increase in age by 1 year increases the risk of LAA thrombosis in men by 5% (odds ratio = 1.05, $p = 0.012$). For each 1-second increase in prothrombin time and INR in men, the risk of LAA thrombus increased by 13 and 293%, respectively (odds ratio = 1.05 and 3.93, respectively, $p < 0.05$).

5. MRI provides high diagnostic accuracy, is safe for patients with allergies to iodine contrast agents or renal failure, and allows for a comprehensive morphofunctional assessment of the heart. MRI is advisable for patients as an alternative to CTA and TEE, as well as for repeated studies, which reduces the radiation load on the patient.

6. A high diagnostic value of the morphological characteristics of the left atrium was established. Patients with a cauliflower-type auricle have a significantly increased risk of thrombus formation ($P<0.001$), which confirms the need to use morphological criteria to predict risk and select therapy, while an increase in the LA volume by 1 ml increased the risk of LAA thrombosis by 2% ($p=0.019$). An increase in the anteroposterior size of the LA by 1 cm increases the risk of LAA thrombus formation by 294% ($p=0.020$). It should be noted that with an increase in the LA volume by 1 ml and the anteroposterior size of the LA by 1 cm, the risk of acute cerebrovascular accident increases by 2 and 78%, respectively.

7. The developed diagnostic algorithms using CTA and MRI significantly improve the quality of diagnostics and treatment of patients with atrial fibrillation, reducing the risk of thromboembolic complications and providing an individualized approach to each patient.

Personal Contribution of the Author

The author contributed by writing the literature review, gathering material, participating in research studies, and interpreting the results. This involved analyzing and summarizing the obtained data, as well as conducting statistical processing. During the collection of literature and scientific materials, the author prepared scientific articles and abstracts for publication. Additionally, the author presented the main findings of the research at international conferences.