

GENDER DIFFERENCES IN PATIENTS WITH ATRIAL FIBRILLATION SHOWN BY TRANSTHORACIC ECHOCARDIOGRAPHY AND COMPUTED TOMOGRAPHY

B.B. KALIYEV¹, R.I. RAKHIMZHANOVA², T.B. DAUTOV¹, L.A. BASTARBEKOVA¹, Zh.A. MOLDAKHANOVA¹, A.M. KABDULLINA³, A.Zh. BIMAKHAN¹

¹NJSC «National Research Cardiac Surgery Center», Nur-Sultan, the Republic of Kazakhstan;

²NJSC «Astana» Medical University, Nur-Sultan, the Republic of Kazakhstan;

³Medical Centre Hospital of President's Affairs Administration of the Republic of Kazakhstan, Nur-Sultan, the Republic of Kazakhstan

ABSTRACT

Relevance: Cardioembolism is one of the major causes of ischemic strokes and accounts for 15-30% of all cerebral infarctions. Atrial fibrillation (AF) accounts for up to 60% of cardioembolic strokes. Assessing thromboembolic risk is important for patients with AF; however, these concerns do not apply equally to men and women.

The study aimed to determine gender differences in echocardiographic and computed tomography characteristics of patients with atrial fibrillation.

Methods: The included 202 patients underwent both transthoracic echocardiography and computed tomography. We excluded patients with allergies to iodide, increased creatinine levels, hyperthyroidism, pregnancy, and age <18 years.

Results: An increase in BMI by 1 kg/m² in female patients increased the risk of left-atrium appendage (LAA) thrombus by 10% (OR=1.1, p=0.019). The yearly increase in the age of women lowers the risk of LAA thrombosis by 6% (OR=0.94, p=0.01). Each increase of EDD in women to 1 cm raises the risk of LAA thrombosis by 151% (OR=2.51, p=0.031). Each increase of ESV and EDV in women to 1 ml raises the risk of LAA thrombosis by 4% and 3%, respectively (p<0.05). Each increase of LVESVI and LVEDVI in female patients to 1 ml/m² raises the risk of LAA thrombosis by 6% and 5%, respectively (p<0.05).

Older age, higher CHA₂-DS₂-VASc, HAS-BLED scores, and enlarger LA in male patients were significantly associated with LAA thrombosis.

The yearly increase in the age of men increases the risk of LAA thrombosis by 5% (OR=1.05, p=0.012). Men with coronary atherosclerosis at risk of thrombosis by 224% (OR=3.24, p=0.002).

Conclusion: Understanding gender differences may help clinicians provide better care to individuals with AF.

Keywords: cardiac CT; atrial fibrillation (AF); echocardiography; gender differences.

Introduction: Cardioembolism is one of the major causes of ischemic strokes and accounts for 15%–30% of all cerebral infarctions. Atrial fibrillation (AF) accounts for ≤60% of cardioembolic strokes. However, the mechanism of stroke development in patients with AF is well known. However, once the patient develops AF, dysrhythmia causes contractile dysfunction and stasis, leading to thrombosis and an increased risk of thromboembolism [1]. Approximately 90% of all thrombi are localized in the left-atrium appendage (LAA) [2-4]. Current therapeutic strategies for AF include both pharmacological and non-pharmacological methods [5]. Electrical cardioversion with radiofrequency pulmonary-vein antral isolation is a practical approach to treating patients with persistent AF [6,7]. However, blood clots in the LAA are a contraindication of electrical cardioversion [8,9]. After normalization of sinus rhythm, restoring contractility and blood flow can lead to a blood clot of the LAA, detachment, and subsequent cardioembolic stroke. Assessing the risk of stroke in patients with AF is very important. Transesophageal cardiography (TEE) remains the gold standard in LAA thrombosis. However, TEE is a semi-inva-

sive procedure with various complications [10]. Computed tomography (CT) is widely used in clinical practice. In addition, recent technology improvements in cardiac CT have increased its attractiveness because it is non-invasive and a viable alternative to TEE [11]. The development of CT-derived criteria indicating an increased risk of LAA thrombosis can be an effective method for diagnosing potential thromboembolisms.

Gender differences in cardiac anatomy and function have not been investigated. This study analyzed structural and hemodynamic differences in transthoracic echocardiography (TTE) and CT between genders by evaluating risk factors for thrombosis in LAA.

Materials and Methods: We conducted a retrospective cohort study by analyzing the records of 202 patients diagnosed with AF. All patients were admitted to the National Research Cardiac Surgery Center from February 2012 to September 2020. All patients underwent both TTE and cardiac CT. The exclusion criteria for CT were allergic reactions to iodide, increased creatinine levels, thyroid disease (hyperthyroidism), pregnancy, and younger age (<18 years old). We divided the patients into four subgroups: 1) all pa-

tients with or without LAA thrombosis, 2) female patients with or without LAA thrombosis, 3) male patients with or without LAA thrombosis, and 4) female and male patients with LAA thrombosis. Congestive heart failure, Hypertension, Age ≥ 75 years, Diabetes mellitus (DM), Stroke or transient ischemic attack, Vascular disease, Age 65 to 74 years, Gender category (CHA₂-DS₂-VASc) and Hypertension, Abnormal renal/liver function, Stroke, Bleeding history or predisposition, Labile international normalized ratio, Elderly, Drugs/alcohol concomitantly (HAS-BLED) scores were calculated in each group. This study was approved by the National Research Cardiac Surgery Center institutional ethics committee and conducted by the Declaration of Helsinki. All patients gave informed consent.

Stroke and bleeding risks were assessed using the CHA₂DS₂-VASc and HAS-BLED scores. The following conditions scored at least one point: history of hypertension, diabetes, congestive heart failure, cardiovascular disease, stroke, transient ischemic attack, or female gender for the CHA₂-DS₂-VASc score.

Hypertension (uncontrolled systolic blood pressure >160 mm Hg), abnormal renal and/or liver function, previous stroke, bleeding history or predisposition, labile international normalized ratios, elderly, concomitant drugs and/or alcohol excess are each assigned 1 point in the HAS-BLED score.

TTE was performed using a Phillips Epiq 7. The study assessed the left-ventricular function (ejection fraction), valve apparatus, and ventricular end-systolic and end-diastolic volumes. Two experienced cardiologists analyzed TTE.

CT scanning was performed on a Siemens Somatom Definition 64 device with retrospective cardio synchronization and reconstruction and a slice thickness of 0.6 mm and a pitch of 0.2 mm. We positioned the patients on their backs and administered intravenous contrast bolus injection using an automatic bolus-free CT injector Ohio Tandem, speed 5 ml/sec, followed by a saline solution of 50 ml. The scan was performed with "bolus tracking" on the ascending aorta at 170 units. At the start of scanning the tracheal bifurcation, the delay after introducing contrast was 10 seconds. Patients were mounted using an ECG synchronizer. The contrast agent dose was calculated based on the patient's weight.

Two experienced radiologists performed the analysis of the CT angiography data. Uniform filling of the LAA was regarded as standard. A defect in the LAA filling was considered a blood clot. The left atrium volume was measured on a Syngo Via workstation using the Volume application along the inner contour of the left atrium, including the LAA manually on each slice. Figure 1 shows an image of the calculation of the left atrium volume. Figure 2 illustrates the LAA thrombosis detected by CT.

Quantitative variables were reported as means and standard deviations. Categorical variables were presented as numbers and percentages in each respective class. Each variable was tested in bivariate analysis with the primary outcome to determine its statistical significance. The Student's t-test and the Mann-Whitney U-test were used for continuous data if the data did not correspond to the parametric test conditions. For qualitative data,

Pearson's chi-square and Fisher's exact tests were made to determine significant associations with the outcome in the two groups. The significance level was set at $\alpha = 0.05$. All statistical analyses were performed using STATA 14.0 software.

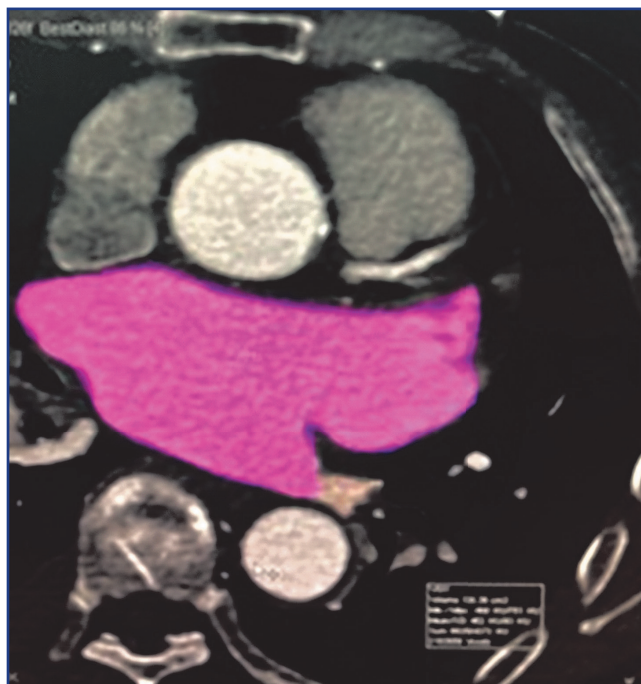


Figure 1 – Calculation of left-atrial volume by computed tomography



Figure 2 – LAA thrombus detected by computed tomography

Results: Overall, 202 patients were enrolled in this study. The mean age of patients was 59.5 (range: 19-86) years. Men accounted for 61.4% of the patients, and the mean Body Mass Index (BMI) was 29.9 kg/m². The mean CHA₂DS₂-VASc score was 2.07 (range: 0–6), and the mean HAS-BLED score was 1.6 (range: 0–5). The average left-atrium volume measured by cardiac CT was 135.2 cm³. See Table 1 for the clinical and demographical characteristics of the patients.

Table 1 – Demographic and medical characteristics of patients (n=202)

Parameter	Mean ± SD or abs. (%)	Standard Deviation (SD) or %
Age, years	59.5	±10.5
Gender		
Female	78	38.6%
Male	124	61.4%
BMI, kg/m ²	29.9	±4.9
CHA ₂ DS ₂ -VASc	2.07	±1.51
HAS-BLED	1.6	±1.22
Coagulogram indicators		
PT, sec	15.7	±5.48
INR, sec	1.3	±0.57
Fibrinogen, g/L	3.35	±2.44
APTT, sec	40.1	±11.4
TTE		
ESD, cm	3.6	±0.75
EDD, cm	4.9	±0.67
ESV, ml	50.6	±30.5
EDV, ml	108	±35.3
SV, ml	54.8	±13.9
LVEF, %	55.6	±9.6
LVESVI, ml/m ²	25.8	±15.5
LVEDVI, ml/m ²	55.2	±17.4
Cardiac CT		
LA volume, cm ³	135.2	±50

Notes: APTT, activated partial thromboplastin time; BMI, Body Mass Index; CT, computed tomography; EDD, end-diastolic dimension; EDV, end-diastolic volume; ESD, end-systolic dimension; ESV, end-systolic volume; LVESVI, left-ventricular end-systolic volume index; LVEDVI, left-ventricular end-diastolic volume index; LVEF, left-ventricular ejection fraction; INR, international normalized ratio; LA, left atrium; PT, prothrombin time; TTE, transthoracic echocardiography.

Higher BMI, higher CHA₂-DS₂-VASc and HAS-BLED scores, and enlarged left atrium and ventricular end-systolic volumes were significantly associated with LAA thrombosis ($p < 0.05$). A higher left-ventricular end-systolic volume measured by TTE predicts LAA thrombosis. After adjustment for the CHA₂DS₂-VASc score, multivariate logistic regression showed that a 1-kg/m² increase in the BMI increased the probability of LAA thrombosis by 10% (odds ratio = 1.1, $p = 0.0092$) (Table 2).

The increased left-ventricular end-systolic volume index by 1 mL/m² enhanced the possibility of blood clot formation by 3%. Although the LAA volume is significantly related to the disease, the odds ratio indicates a slight difference (odds ratio = 1.014, $p = 0.000$) (Table 2). End systolic and diastolic dimensions of the left ventricle measured by TTE are shown in Figures 3 & 4.



Figure 3 – End-diastolic dimension of left ventricle measured on TTE

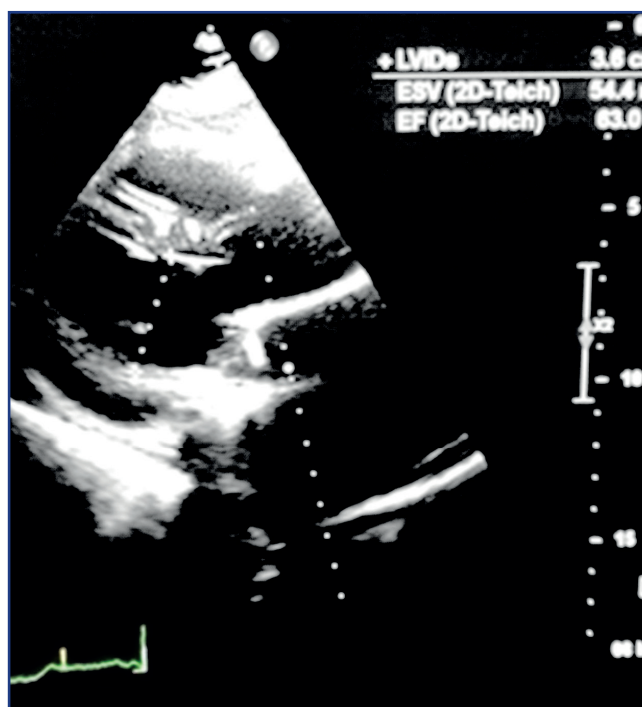


Figure 4 – End-systolic dimension of left ventricle measured on TTE

Table 2 – Demographic and medical characteristics of patients with or without LAA thrombosis

Parameter	No LAA thrombosis, mean ± SD, or abs. (%) (n=100)	LAA thrombosis, mean ± SD or abs. (%) (n=102)	p-value	Females, abs. (%) (n=41)	Males, abs. (%) (n=61)	p-value
Age, years	59.2 (10.7)	59.8 (10.3)	0.73	59 (10.8)	60 (10.9)	0.54
Gender			0.64			
Female	37 (47.4%)	41 (52.6%)				
Male	63 (50.8%)	61 (49.2%)				
BMI, kg/m ²	28.8 (4.8)	31 (4.8)	0.0092	32.5 (3.8)	29.9 (5.1)	0.019
CHA ₂ DS ₂ -VASc	1.7 (1.4)	2.45 (1.5)	0.0003	2.54 (1.5)	2.39 (1.5)	0.64
HAS-BLED	1.24 (1.1)	1.94 (1.3)	<0.0001	1.76 (1.2)	2.07 (1.3)	0.23

Table 3 (continued)

Coagulogram indicators						
PT, sec	14.7 (4.8)	16.6 (6)	0.015	16.7 (6.8)	16.6 (5.4)	0.91
INR, sec	1.21 (0.4)	1.4 (0.7)	0.021	1.39 (0.8)	1.4 (0.59)	0.97
Fibrinogen, g/L	3.1 (0.7)	3.6 (3.4)	0.18	4.2 (5.2)	3.2 (0.96)	0.15
APTT, sec	39.9 (11.3)	40.4 (11.5)	0.75	38.2 (13.2)	41.8 (10.1)	0.13
TTE						
ESD, cm	3.5 (0.68)	3.6 (0.82)	0.34	3.54 (0.82)	3.7 (0.82)	0.28
EDD, cm	4.8 (0.61)	4.95 (0.72)	0.19	4.9 (0.63)	5 (0.8)	0.41
ESV, ml	46.2 (18.1)	54.9 (38.7)	0.041	49 (26)	59 (45)	0.21
EDV, ml	105 (32)	111 (38.1)	0.21	109 (37.9)	112.8 (38.6)	0.63
SV, ml	54.5 (13.4)	55.3 (14.5)	0.72	51.8 (11.7)	56.8 (15.5)	0.24
LVEF, %	56.4 (7.1)	54.1 (11.2)	0.09	54.6 (13.7)	53.6 (9.3)	0.66
LVESVI, ml/m ²	23.5 (8.7)	28.04 (19.9)	0.042	26.3 (14)	29.3 (23.2)	0.47
LVEDVI, ml/m ²	53.5 (14.4)	56.9 (19.8)	0.17	58.2 (18.1)	56.1 (21)	0.61
Cardiac CT						
LA volume, cm ³	119.4 (44.8)	150.71 (50.3)	0.0001	145.3 (59)	153.1 (44.4)	0.51

Notes: APTT, activated partial thromboplastin time; BMI, Body Mass Index; CT, computed tomography; EDD, end-diastolic dimension; EDV, end-diastolic volume; ESD, end-systolic dimension; ESV, end-systolic volume; LVESVI, left-ventricular end-systolic volume index; LVEDVI, left-ventricular end-diastolic volume index; LVEF, left-ventricular ejection fraction; INR, international normalized ratio; LA, left atrium; PT, prothrombin time; TTE, transthoracic echocardiography.

History of hypertension was found in 69.8% of the participants, 52.5% of patients had a history of atherosclerosis, only two patients had DM, and the number of patients with low left-ventricular fraction was 10 (5%) (Table 3). Evaluation of the valve apparatus showed a significant association with LAA thrombosis in patients with mitral valve regurgitation ($p=0.041$). Comorbidities analysis showed a 152% higher risk of thrombosis in coronary atherosclerosis patients (odds ratio =2.52, $p=0.001$) (Table 4).

Table 3 – Comorbidities and forms of atrial fibrillation in the total cohort (n=202)

Parameter	Abs.	%
Hypertension	141	69.8
Coronary sclerosis	106	52.5
DM	4	2
Heart failure		
LVEF < 40%	10	5
40% ≤ LVEF ≤ 49%	31	15.3
LVEF ≥ 50%	161	79.7
Mitral valve evaluation		
normal	179	88.6
regurgitation	23	11.4
Atrial fibrillation		
paroxysmal	68	33.7
persistent	75	37
long-term persistent	39	19.3
permanent	20	10

Notes: LVEF, left ventricular ejection fraction; DM, diabetes mellitus.

Multivariate logistic regression showed that a 1-kg/m² increase in BMI increased the risk of LAA thrombosis in female patients by 10% (odds ratio =1.1, $p=0.019$) (Table 5).

Table 4 – Comorbidities in patients with or without LAA thrombosis

Parameter	No LAA thrombosis, abs. (%) (n=100)	LAA thrombosis, abs. (%) (n=102)	p-value	Females, abs. (%) (n=41)	Males, abs. (%) (n=61)	p-value
Hypertension	67 (47.5%)	74 (52.5%)	0.39	30 (40.5%)	44 (59.5%)	0.91
Coronary sclerosis	41 (38.7%)	65 (61.3%)	0.001	21 (32.3%)	44 (67.7%)	0.031
DM	3 (75%)	1 (25%)	0.3	1 (100%)	0	0.22

TTE and CT characteristics did not show significant differences between male and female patients with thrombus in LAA (Table 2). Analysis of concurrent illnesses showed that male patients with coronary atherosclerosis had a 146% increased risk of thrombosis (OR= 2.46, $p= 0.031$) (Table 4).

Increasing age lowered the risk of LAA thrombosis by 6% in women (odds ratio =0.94, $p= 0.01$). Each 1-cm increase in end-diastolic dimension in women increased the risk of LAA thrombosis by 151% (odds ratio = 2.51, $p=0.031$) (Table 5). Each 1-ml increase in the ventricular end-systolic volume and end-diastolic volume in women increased the risk of LAA thrombosis by 4% and 3%, respectively ($p>0.05$) (Table 5). Each 1 ml/m²-increase in the left-ventricular end-systolic volume and left-ventricular end-diastolic volume in women increased the risk of LAA thrombosis by 6% and 5%, respectively ($p>0.05$) (Table 5). Mitral valve insufficiency in female patients was significantly associated with LAA thrombosis ($p>0.05$) (Table 6).

Older age, higher CHA₂-DS₂-VASc and HAS-BLED scores, and enlarged left atrium in males were significantly associated with LAA thrombosis ($p<0.05$) (Table 7).

Increased age increased the risk of LAA thrombosis in men by 5% (odds ratio=1.05, $p=0.012$) (Table 7). With each 1-second increase in the prothrombin time and international normalized ratio in men, the risk of LAA thrombosis increased by 13% and 293%, respectively (odds ratio=1.05 and 3.93, respectively, $p<0.05$) (Table 7). There were no significant differences in the TTE characteristics between male patients with or without LAA thrombosis. Analysis of concurrent illnesses showed that men with coronary atherosclerosis had a 224% higher risk of thrombosis (odds ratio=3.24, $p=0.002$) (Table 8).

Table 4 (continued)

Heart failure			0.087		0.83
LVEF<40%	2 (20%)	8 (80%)		3 (37.5%)	5 (62.5%)
40%≤LVEF≤49%	13 (42%)	18 (58%)		6 (33.3%)	12 (66.7%)
LVEF≥50%	85 (52.8%)	76 (47.2%)		32 (42.1%)	44 (57.9%)
Valve apparatus estimation			0.041		0.41
Normal	84 (46.9%)	95 (53.1%)		39 (41%)	56 (59%)
Mitral valve regurgitation	16 (69.6%)	7 (30.4%)		2 (28.6%)	5 (71.4%)
Atrial fibrillation					0.65
paroxysmal				12 (48%)	13 (52%)
persistent				17(42.5%)	23(57.5%)
long-term persistent				7 (30.4%)	16(69.6%)
permanent				5 (35.7%)	9 (64.3%)

Notes: LVEF, left-ventricular ejection fraction; DM, diabetes mellitus.

Table 5 – Demographic and medical characteristics of female patients (n=78)

Parameter	No LAA thrombosis, abs. (%) (n=37)	LAA thrombosis, abs. (%) (n=41)	p-value
Age, years	65.2 (9.7)	59 (10.8)	0.01
BMI, kg/m ²	30.2 (5.9)	32.5 (3.8)	0.09
CCHA ₂ DS ₂ -VASc	1.92 (1.6)	2.54 (1.5)	0.08
HAS-BLED	1.46 (1.1)	1.76 (1.2)	0.26
Coagulogram indicators			
PT, sec	15.4 (6.5)	16.7 (6.8)	0.43
INR, sec	1.31 (0.62)	1.39 (0.78)	0.61
Fibrinogen, g/L	3.3 (0.6)	4.2 (5.2)	0.31
APTT, sec	41.7 (13.9)	38.2 (13.2)	0.26
TTE			
ESD, cm	3.32 (0.77)	3.54 (0.82)	0.22
EDD, cm	4.57 (0.6)	4.88 (0.63)	0.027
ESV, ml	36.5 (14.5)	49 (26.2)	0.012
EDV, ml	84.9 (24)	109 (37.9)	0.001
SV, ml	45.9 (10.5)	51.8 (11.7)	0.09
LVEF, %	58 (7.6)	54.6 (13.7)	0.19
LVESVI, ml/m ²	20.4 (7.6)	26.3 (13.9)	0.03
LVEDVI, ml/m ²	47.6 (12.4)	58.2 (18.1)	0.005
Cardiac CT			
LA volume, cm ³	111.3 (41.8)	145.3 (59)	0.013

Notes: APTT, activated partial thromboplastin time; BMI, Body Mass index; CT, computed tomography; EDD, end-diastolic dimension; EDV, end-diastolic volume; ESD, end-systolic dimension; ESV, end-systolic volume; LVESVI, left-ventricular end-systolic volume index; LVEDVI, left-ventricular end-diastolic volume index; LVEF, left-ventricular ejection fraction; INR, international normalized ratio; LA, left atrium; PT, prothrombin time; TTE, transthoracic echocardiography.

Table 6 – Comorbidities in female patients (n=78)

Parameter	No LAA thrombosis (n=37)	LAA thrombosis (n=41)	p-value
Hypertension	28 (48.3%)	30 (51.7%)	0.80
Coronary sclerosis	13 (38.2%)	21 (61.8%)	0.15
DM	2 (66.7%)	1 (33.3%)	0.60
Heart failure			0.67
LVEF<40%	1 (25%)	3 (75%)	
40%≤LVEF≤49%	4 (40%)	6 (60%)	
LVEF≥50%	32 (50%)	32 (50%)	
Valve apparatus estimation			0.02
Normal	28 (41.8%)	39 (58.2%)	
Regurgitation	9 (81.8%)	2 (18.2%)	
Atrial fibrillation			0.22
paroxysmal	19 (61.3%)	12 (38,7%)	
persistent	10 (37%)	17 (63%)	
long-term persistent	6 (46.2%)	7 (53.8%)	
permanent	2 (28.6%)	5 (71.4%)	

Notes: LVEF, left-ventricular ejection fraction; DM, diabetes mellitus.

Table 7 – Demographic and medical characteristics of male patients (n=124)

Parameter	No LAA thrombosis, abs. (%) (n=63)	LAA thrombosis, abs. (%) (n=61)	p-value
Age, years	55.7 (9.7)	60.3 (10)	0.012
BMI, kg/m ²	28.13 (3.9)	29.9 (5.1)	0.06
CHA ₂ DS ₂ -VASc	1.57 (1.35)	2.39 (1.5)	0.002
HAS-BLED	1.11 (1.1)	2.1 (1.3)	<0.0001
Coagulogram indicators			
PT, sec	14.3 (3.4)	16.5 (5.4)	0.006
INR, sec	1.15 (0.3)	1.39 (0.6)	0.003
Fibrinogen, g/L	3.02 (0.7)	3.19 (0.9)	0.25
APTT, sec	38.8 (9.4)	41.8 (10.2)	0.09
TTE			
ESD, cm	3.68 (0.6)	3.72 (0.8)	0.76
EDD, cm	4.9 (0.6)	5 (0.8)	0.90
ESV, ml	51.9 (17.6)	59 (45)	0.25
EDV, ml	116.9 (30.3)	112.8 (38.6)	0.51
SV, ml	59.5 (12.4)	56.8 (15.5)	0.37
LVEF, %	55.5 (6.8)	53.6 (9.3)	0.21
LVESVI, ml/m ²	25.3 (8.9)	29.3 (23.2)	0.21
LVEDVI, ml/m ²	56.9 (14.5)	56.1 (21)	0.81
Cardiac CT			
LA volume, cm ³	124.4 (46.3)	153.1 (44.4)	0.003

Notes: APTT, activated partial thromboplastin time; BMI, Body Mass Index; CT, computed tomography; EDD, end-diastolic dimension; EDV, end-diastolic volume; ESD, end-systolic dimension; ESV, end-systolic volume; LVESVI, left-ventricular end-systolic volume index; LVEDVI, left-ventricular end-diastolic volume index; LVEF, left-ventricular ejection fraction; INR, international normalized ratio; LA, left atrium; PT, prothrombin time; TTE, transthoracic echocardiography.

Table 8 – Comorbidities in male patients (n=124)

Parameter	No LAA thrombosis, abs. (%) (n=63)	LAA thrombosis, abs. (%) (n=61)	p-value
Hypertension	39 (47%)	44 (53%)	0.23
Coronary sclerosis	28 (38.9%)	44 (61.1%)	0.002
DM	1 (100%)	0	0.32
Heart failure			0.13
LVEF < 40%	1 (16.7%)	5 (83.3%)	
40% ≤ LVEF ≤ 49%	9 (42.9%)	12 (57.1%)	
LVEF ≥ 50%	53 (54.6%)	44 (45.4%)	
Valve apparatus estimation			0.76
Normal	56 (50%)	56 (50%)	
Regurgitation	7 (58.3%)	5 (41.7%)	
Atrial fibrillation			0.08
paroxysmal	24 (64.9%)	13 (35.1%)	
persistent	25 (52.1%)	23 (47.9%)	
long-term persistent	10 (38.5%)	16 (61.5%)	
permanent	4 (30.8%)	9 (69.2%)	

Notes: LVEF, left-ventricular ejection fraction; DM, diabetes mellitus

Discussion: Female gender continues to be recognized as a stroke risk factor in AF [12]. Previous studies have reported several gender-related differences in the prevalence, clinical presentation, associated comorbidities, and therapeutic outcomes of patients with AF [13]. This study found that TTE measured enlarged left-atrial volume and end-systolic left-ventricular volume. TTE was independently associated with LAA thrombosis detected by cardiac CT in patients with a history of AF and receiving anticoagulant therapy in the total cohort. This finding was factual even when adjusted for BMI and CHA₂DS₂-VASc score. The left-ventricular ejection fraction was not significantly associated with LAA thrombosis, most likely because of the low share of heart failure patients; in most patients, the ejection fraction was high. However, an increased left-ventricular end-diastolic volume index remained significant in predicting LAA thrombosis in female patients.

It was previously reported that increased left-atrial systolic and diastolic volume indexes were independently associ-

ated with LAA thrombosis in patients with AF [14]. Left-atrial volume is an independent risk factor for various cardiovascular events and is associated with coronary sclerosis, with an increased risk of ischemic stroke and myocardial infarction [15,16]. In addition, an increase in the left-atrium volume is often associated with a relapse of AF after radiofrequency ablation [17]. In all groups of patients, enlarged LA measured by CT was strongly related to the presence of LAA thrombosis.

Additionally, women with AF are more likely than males to develop valvular heart disease and heart failure with retained left-ventricular function. Still, they have a lower risk of coronary artery disease [18]. Simultaneously, coronary atherosclerosis was significantly associated with an increased risk of thrombosis of the LAA, $p=0.001$, with a higher risk of LAA thrombosis in men.

We found that the CHA₂DS₂-VASc score had a statistically significant association with LAA thrombosis in male patients ($p=0.0003$) but not in female patients. However, in the study, increasing age lowered the risk of LAA thrombosis in women by 6%, probably because of their young age.

The association between AF and obesity has been previously studied in patients with cardiac pathologies. Since then, several epidemiological studies have found a strong association between obesity and AF [19]. In our study, an increased BMI correlated with the risk of LAA thrombosis (odds ratio=1.1, $p=0.0092$).

Cardiac CT also allows for evaluating and treating AF and assessing the location, size, and number of pulmonary veins before ablation. CT's high diagnostic accuracy can also determine the coronary arteries and coronary sclerosis anatomy and exclude LAA thrombosis in patients with AF.

Our study had several limitations. First, this was a single-center study. Women's risk of developing an LAA thrombosis decreased with increasing age per year. Although the present analysis included 202 patients, there were still limitations in the sample of patients because of their relatively young age. Second, in our center, measurements of the linear dimensions and volumes of the left ventricle were performed only by TTE. Because the echocardiograms were gathered from existing hospital records in the research location, they were not interpreted systematically; nonetheless, these data reflect actual clinical practice. This study did not provide CT to evaluate the left ventricle's dimensions and volumes, indicating the need for further research.

Conclusion: It can be inferred that specific gender differences are evident in echocardiography and CT data, which may reflect hemodynamic and structural abnormalities in individuals with AF. Our findings demonstrate that TTE and cardiac CT provide beneficial information for predicting thrombosis formation risks in LAA. Thus, it is necessary to consider age, gender, and concurrent illnesses. Improved clinician understanding of these gender differences may aid in caring for patients with AF. The study results invite further research since. However, there are many gaps in our knowledge concerning this issue.

References

1. Kamel H, Okin P.M., Elkind M.S., Iadecola C. Atrial fibrillation and mechanisms of stroke: time for a new model // *Stroke*. – 2016. – Vol. 47. – P. 898-900. <https://doi.org/10.1161/STROKEAHA.115.012004>;
2. 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. – Vol. 7. – P. 199-203. <https://doi.org/10.3978/j.issn.2072-1439.2015.01.20>;
3. Syed F.F., DeSimone C.V., Friedman P.A., Asirvatham S.J. Left atrial appendage exclusion for atrial fibrillation // *Cardiol Clin.* – 2014. – Vol. 32. – P. 601-625. <https://doi.org/10.1016/j.ccl.2014.07.006>;
4. Mahajan R., Brooks A.G., Sullivan T., Lim H.S., Alasady M., Abed H.S., Ganesan A.N., Nayyar S., Lau D.H., Roberts-Thomson K.C., Kalman J.M. Importance of the underlying substrate in determining thrombus location in atrial fibrillation: implications for left atrial appendage closure // *Heart*. – 2012. – Vol. 98. – P. 1120-1126. <https://doi.org/10.1136/heartjnl-2012-301799>;

5. Xu J, Luc J.G.Y., Phan K. Atrial fibrillation: a review of current treatment strategies // *J. Thorac Dis.* – 2016. – Vol. 8. – P. E886-E900. <https://doi.org/10.21037/jtd.2016.09.13>;
6. Brandes A., Crijns H.J., Rienstra M., Kirchhof P., Grove E.L., Pedersen K.B., Van Gelder I.C. Cardioversion of atrial fibrillation and atrial flutter revisited: current evidence and practical guidance for a standard procedure // *Europace*. – 2020. – Vol. 22. – P. 1149-1161. <https://doi.org/10.1093/europace/eaad057>;
7. Kojodjojo P., D. O'Neill M., Lim P.B., Malcolm-Lawes L., Whinnett Z.I., Salukhe T.V., Linton N.W., Lefroy D., Mason A., Wright I., Peters N.S. Pulmonary venous isolation by antral ablation with a large cryo-balloon for treatment of paroxysmal and persistent atrial fibrillation: medium-term outcomes and non-randomized comparison with pulmonary venous isolation by radiofrequency ablation // *Heart*. – 2010. – Vol. 96. – P. 1379-1384. <https://doi.org/10.1136/hrt.2009.192419>;
8. Squara F., Bres B., Scarlatti D., Moceri P., Ferrari E. Clinical Outcomes after AF Cardioversion in patients presenting left atrial sludge in trans-esophageal echocardiography // *J. Interv. Card. Electrophysiol.* – 2020. – Vol. 57. – P. 149-156. <https://doi.org/10.1007/s10840-019-00561-8>;
9. Melillo E., Palmiero G., Ferro A., Moccavero P.E., Monda V., Ascione L. Diagnosis and management of left atrium appendage thrombosis in atrial fibrillation patients undergoing cardioversion // *Medicine*. – 2019. – Vol. 55. – P. 511. <https://doi.org/10.3390/medicine55090511>;
10. Purza F., Ghosh S., Walker C., Hiebert B., Koley L., Mackenzie G.S., Grocott H.P. Transesophageal echocardiography complications in adult cardiac surgery: a retrospective cohort study // *Ann Thorac Surg.* – 2017. – Vol. 103. – P. 795-802. <https://doi.org/10.1016/j.athoracsurg.2016.06.073>;
11. Budoff M.J., Shittu A., Hacıoglu Y., Gang E., Li D., Bhatia H., Alvergue J., Karlsberg R.P. Comparison of transesophageal echocardiography versus computed tomography for detection of left atrial appendage filling defect (thrombus) // *Am. J. Cardiol.* – 2014. – Vol. 113. – P. 173-177. <https://doi.org/10.1016/j.amjcard.2013.09.037>;
12. Cheng E.Y., Kong M.H. Gender differences of thromboembolic events in atrial fibrillation // *Am J. Cardiol.* – 2016. – Vol. 117. – P. 1021-1027. <https://doi.org/10.1016/j.amjcard.2015.12.040>;
13. Odening K.E., Deiß S., Dilling-Boer D., Didenko M., Eriksson U., Nedios S., Ng F.S., Roca Luque I., Sanchez Borque P., Vernooy K., Wijnmaalen A.P. Mechanisms of gender differences in atrial fibrillation: role of hormones and differences in electrophysiology, structure, function, and re-modelling // *E.P. Europace*. – 2019. – Vol. 21. – P. 366-376. <https://doi.org/10.1093/europace/euy215>;
14. Osawa K., Nakanishi R., Ceponiene I., Nezarat N., French W.J., Budoff M.J. Predicting Left atrial appendage thrombus from left atrial volume // *Tex Heart Inst. J.* – 2020. – Vol. 47. – P. 78-85. <https://doi.org/10.14503/THIJ-17-6290>;
15. Facchini E., Degiovanni A., Paolo N. Marin Left atrium function in patients with coronary artery disease // *Curr. Opin. Cardiol.* – 2014. – Vol. 29. – P. 423-429. <https://doi.org/10.1097/HCO.0000000000000085>;
16. Xu Y., Zhao L., Zhang L., Han Y., Wang P., Yu S. Left atrial enlargement and the risk of stroke: a meta-analysis of prospective cohort studies // *Front Neurol.* – 2020. – Vol. 14. – P. 26. <https://doi.org/10.3389/fneur.2020.00026>;
17. Kim Y.G., Shim J., Oh S.K., Park H.S., Lee K.N., Hwang S.H., Choi J.I., Kim Y.H. Different responses of the left atrium and left atrial appendage to radiofrequency catheter ablation of atrial fibrillation: a follow-up MRI study // *Sci. Rep.* – 2018. – Vol. 8. – P. 1-9. <https://doi.org/10.1038/s41598-018-26212-y>;
18. Dagues N., Nieuwlaat R., Vardas P.E., Andresen D., Lévy S., Cobbe S., Kremastinos D.T., Breithardt G., Cokkinos D.V., Crijns H.J. Gender-related differences in presentation, treatment, and outcome of patients with atrial fibrillation in Europe // *J. Am. Coll. Cardiol.* – 2007. – Vol. 49. – P. 572-577. <https://doi.org/10.1016/j.jacc.2006.10.047>;
19. Vyas V., Lambiase P. Obesity and atrial fibrillation: epidemiology, pathophysiology and novel therapeutic opportunities // *Arrhythm. Electrophysiol. Rev.* – 2019. – Vol. 8. – P. 28-36. <https://doi.org/10.15420/aer.2018.76.2>.

ТУЖЫРЫМ

ТРАНСТОРАКАЛЬДЫ ЭХОКАРДИОГРАФИЯ ЖӘНЕ КОМПЬЮТЕРЛІК ТОМОГРАФИЯ АРҚЫЛЫ АНЫҚТАЛҒАН ЖҮРЕКШЕЛЕРДІҢ ФИБРИЛЛЯЦИЯСЫ БАР НАУҚАСТАРДАҒЫ ЖЫНЫСТЫҚ АЙЫРМАШЫЛЫҒЫ

Б.Б. Калиев¹, Р.И. Рахимжанова², Т.Б. Даутов¹, Л.А. Бастарбекова¹, Ж.А. Молдаханова¹, А.М. Кабдуллина³, А.Ж. Бимахан¹

¹«Ұлттық Ғылыми Кардиохирургиялық орталық» КеАҚ, Нұр-Сұлтан, Қазақстан Республикасы;

²«Астана» медицина университеті КеАҚ, Нұр-Сұлтан, Қазақстан Республикасы;

³Қазақстан Республикасы Президентінің Іс Басқармасы Медициналық орталығының ауруханасы, Нұр-Сұлтан, Қазақстан Республикасы

Өзектілігі: Кардиоэмболия ишемиялық инсульттің негізгі себептерінің бірі болып табылады және барлық церебральды инфаркттардың 15-30% құрайды. Жүрекшелердің фибрилляциясы (АФ) кардиоэмболиялық инсульттердің 60% құрайды. Тромбоэмболия қаупін

бағалау жүрекішелердің фибрилляциясы бар науқастар үшін маңызды; дегенмен, бұл алаңдаушылықтар ерлер мен әйелдерге бірдей қауіпті емес.

Зерттеудің мақсаты жүрекішелердің фибрилляциясы бар науқастарда эхокардиографиялық және компьютерлік томографиялық сипаттамалардағы гендерлік айырмашылықтарды анықтау болып табылады.

Әдістері: Барлық науқасқа трансторакальды эхокардиография мен компьютерлік томография жасалды (КТ). Йод аллергиясы, жоғары креатинин, гипертиреоз, жүктілік, жасы <18 жасан төмен науқастар топқа қосылмады.

Нәтижелер. Әйел науқастарында дене салмағының индексі 1 кг/м^2 артуы сол жүрекішенің құлақшасы тромбозының қаупін 10%-ға арттырды ($OR=1,1, p=0,019$). Әйелдер жасының 1 жылға артуы сол жүрекішенің құлақшасы тромбозының қаупін 6%-ға төмендетеді ($OR=0,94, p=0,01$). Әйелдердегі шекті диастоликалық диаметр әрбір 1 см жоғарылауы сол жүрекішенің құлақшасы тромбозының қаупін 151% арттырады ($OR=2,51, p=0,031$). Әйелдерде шекті диастоликалық көлемінің және шекті систоликалық көлемінің 1 мл-ге артуы, сәйкесінше, 4% және 3%-ға сол жүрекішенің құлақшасы тромбозының қаупін арттырады ($p<0,05$). Әйел жынысты пациенттерде индекстелген шекті диастоликалық және шекті систоликалық көлемінің 1 мл/м²-ге әрбір ұлғаюы сол жүрекішенің құлақшасы тромбоз қаупін тиісінше 6% және 5%-ға арттырады ($p<0,05$).

Егде жас, жоғары CHA_2DS_2-VASc , $HAS-BLED$ көрсеткіштері және ер пациенттерде сол жүрекішенің ұлғаюы сол жүрекішенің құлақшасының тромбымен айтарлықтай байланысты.

Ерлердің жасының 1 жылға артуы сол жүрекішенің құлақшасы тромбозының қаупін 5%-ға арттырады ($OR=1,05, p=0,012$). Қоронарлық атеросклерозы бар ерлерде тромб түзілу қаупі – 224% ($OR=3,24, p=0,002$).

Қорытынды: Клиницисттердің гендерлік айырмашылықтарды жақсы түсінуге жүрекішелер фибрилляциясы бар адамдарда емдеу деңгейін жоғарлатуға үлесін қосуы мүмкін.

Түйінді сөздер: жүректің КТ; жүрекішелердің фибрилляциясы; эхокардиография; гендерлік айырмашылықтар

АННОТАЦИЯ

ГЕНДЕРНЫЕ РАЗЛИЧИЯ У ПАЦИЕНТОВ С ФИБРИЛЛЯЦИЕЙ ПРЕДСЕРДИЙ, ВЫЯВЛЕННОЙ С ПОМОЩЬЮ ТРАНСТОРАКАЛЬНОЙ ЭХОКАРДИОГРАФИИ И КОМПЬЮТЕРНОЙ ТОМОГРАФИИ

Б.Б. Калиев¹, Р.И. Рахимжанова², Т.Б. Даутов¹, Л.А. Бастарбекова¹, Ж.А. Молдаханова¹, А.М. Кабдуллина³, А.Ж. Бимахан¹

¹НАО «Национальный научный кардиохирургический центр», Нур-Султан, Республика Казахстан;

²НАО Медицинский университет «Астана», Нур-Султан, Республика Казахстан;

³Больница Медицинского центра Управления Делами Президента Республики Казахстан, Нур-Султан, Республика Казахстан

Актуальность: Кардиоэмболия является одной из основных причин ишемических инсультов и составляет 15-30% всех инфарктов головного мозга. На долю фибрилляции предсердий приходится до 60% кардиоэмболических инсультов. Оценка риска тромбоза эмболии важна для пациентов с мерцательной аритмией, однако эти опасения не относятся в равной степени к мужчинам и женщинам.

Целью исследования было определение гендерных различий у больных с фибрилляцией предсердий по данным трансторакальной эхокардиографии и компьютерной томографии.

Методы: Всем пациентам была проведена как трансторакальная эхокардиография, так и компьютерная томография. Из исследования были исключены пациенты с аллергией на йод, повышенным уровнем креатинина, гипертиреозом, беременностью, возрастом <18 лет.

Результаты: Увеличение индекса массы тела на 1 кг/м^2 у женщин повышало риск тромбоза ушка левого предсердия (УЛП) на 10% (отношение шансов (ОШ)=1,1, $p=0,019$). С каждым увеличением возраста женщины на 1 год риск тромбоза УЛП снижался на 6% ($OR=0,94, p=0,01$). Каждое увеличение конечного диастолического размера у женщины на 1 см повышало риск тромбоза УЛП на 151% ($OR=2,51, p=0,031$). Каждое увеличение конечного систолического объема (КСО) и конечного диастолического объема (КДО) у женщины на 1 мл повышало риск тромбоза УЛП на 4% и 3%, соответственно ($p<0,05$). Каждое увеличение индексированных КСО и КДО левого желудочка у женщины на 1 мл/м^2 повышало риск тромбоза УЛП на 6% и 5%, соответственно ($p<0,05$).

Пожилые возраст, более высокие баллы CHA_2DS_2-VASc , $HAS-BLED$ и увеличение объема левого предсердия у мужчин были в значительной степени связаны с тромбом УЛП. Увеличением возраста мужчин на 1 год повышалось риск тромбоза УЛП на 5% ($OR=1,05, p=0,012$). Коронарный атеросклероз повышал риск тромбообразования у мужчин на 224% ($OR=3,24, p=0,002$).

Заключение: Понимание гендерных различий может помочь клиницистам лучше заботиться о людях с фибрилляцией предсердий.

Ключевые слова: компьютерная томография сердца; фибрилляция предсердий (ФП); эхокардиография; гендерные различия

Transparency of the study: Authors take full responsibility for the content of this manuscript.

Conflict of interests: Authors declare no conflict of interest.

Financing: Authors declare no financing of the study.

Authors' input: contribution to the study concept – Rakhimzhanova R.I., Dautov T.B.; study design – Kaliyev B.B.; execution of the study – Bastarbekova L.A.; interpretation of the study – Moldakhanova Zh.A., Kabdullina A.M.; preparation of the manuscript – Bimakhan A.Zh., Kaliyev B.B.

Authors' data:

Kaliyev B.B. (corresponding author) – M.D., Department of Radiology of National Research Cardiac Surgery Center, Turan Avenue 38, Nur-Sultan, 010000, the Republic of Kazakhstan, tel. +77014011358, e-mail: baur233113@mail.ru, ID ORCID: <https://orcid.org/0000-0003-4825-749X>;

Rakhimzhanova R.I. – Honored Worker of the RK, Academician of the Academy of Preventive Medicine of the RK, Head of the Department of Radiology No. 1 of JSC "Astana Medical University", Nur-Sultan, the Republic of Kazakhstan, tel. +77012288058, e-mail: rakhimzhanova01@rambler.ru, ID ORCID: <https://orcid.org/0000-0002-3490-6324>;

Dautov T.B. – Doctor of Science, M.D., Ph.D., Ass. Prof, Head of the Department of Radiology and Nuclear Medicine, Corporate fund "University Medical Center", Nur-Sultan, the Republic of Kazakhstan, tel. +77077713367, e-mail: tairkhan.dautov@mail.ru, ID ORCID: <https://orcid.org/0000-0002-5267-0108>;

Bastarbekova L.A. – M.D., M.Sc., Department of Radiology, National Research Cardiac Surgery Center MOH RK, Nur-Sultan, the Republic of Kazakhstan, tel. +77022844036, e-mail: lbastarbekova@mail.ru, ID ORCID: <https://orcid.org/0000-0001-8246-4754>;

Moldakhanova Zh.A. – M.D., Department of Radiology, National Research Cardiac Surgery Center MOH RK, Nur-Sultan, the Republic of Kazakhstan, tel. +77716066716, e-mail: moldahanova1991@mail.ru, ID ORCID: <https://orcid.org/0000-0002-5980-9563>;

Kabdullina A.M. – M.D., Department of Nuclear Medicine, Medical Centre Hospital of President's Affairs Administration of the Republic of Kazakhstan, Nur-Sultan, the Republic of Kazakhstan, tel. +77760108877, e-mail: azharazh@mail.ru, ID ORCID: <https://orcid.org/0000-0003-0521-5484>;

Bimakhan A.Zh. – M.D., Department of Radiology, National Research Cardiac Surgery Center MOH RK, Nur-Sultan, the Republic of Kazakhstan, tel. +77757355995, e-mail: abimakhan95@gmail.com, ID ORCID: <https://orcid.org/0000-0003-3100-3389>.