SHORT COMMUNICATION

The rationale and design of the LATTEE registry – the first multicenter project on the Scientific Platform of the "Club 30" of the Polish Cardiac Society

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Introduction Since its establishment 25 years ago, the "Club 30" of the Polish Cardiac Society has gathered young Polish scientists with meaningful achievements in cardiology.[1] The "Club 30" Scientific Platform has been created to facilitate initiation of and participation in multicenter studies among its users, and to promote integration of scientific community.[2] Multicenter cooperation, empowered by the platform, results in an increase in the number of enrolled patients and, consequently, enhances research quality and chances for publication in high-profile journals.

In patients with atrial fibrillation (AF) and atrial flutter (AFl), oral anticoagulation (OAC) reduces the risk of both left atrial (LA) thrombus and ischemic stroke.[3-5] Yet, some patients develop LA thrombus and experience thromboembolic events despite OAC.[6-9] The CHA_2DS_2-VASc-RAF (congestive heart failure, hypertension, age ≥75 years, diabetes mellitus, history of stroke or thromboembolism, vascular disease, age 65 to 74 years, female sex, renal dysfunction, type of AF) score has been recently proposed to improve LA thrombus prediction in AF.[9]

The aim of the study is to assess the prevalence of LA thrombus in real-world patients with AF or AFl referred for transesophageal echocardiography (TEE), to identify predictors

of LA thrombus in these patients, and to validate the CHA_2DS_2-VASc-RAF score.

Methods The LATTEE registry (Left Atrial Thrombus on Transesophageal Echocardiography; ClinicalTrials.gov identifier, NCT03591627) is an ongoing multicenter prospective observational study, conducted in 13 Polish cardiology centers. The registry includes all consecutive patients with AF or AFl hospitalized in a participating center during the study period, who were scheduled for catheter ablation or cardioversion for AF or AFl and had TEE performed prior to the procedure (irrespective of whether the procedure was finally carried out or not). The exclusion criteria are age below 18 years and inconclusive TEE results regarding the presence of LA thrombus. Patients are enrolled in the study irrespective of the presence or type of OAC. Each of the 13 participating centers will include at least 200 patients. Thus, the total number of patients in the registry is estimated to exceed 2600. In each participating center, recruitment will last 12 months, starting from the date of enrollment of the first patient in this center, or longer if the required number of 200 patients is not reached by the participating center within 12 months.

In all patients, data on clinical characteristics, pharmacotherapy, routine blood tests, and TEE results are collected. All other tests are performed at the di scretion of the attending physician within the standards of care in a given center. However, if available, data from transthoracic echocardiography and Holter monitoring are also recorded (TABLE 1). If a patient undergoes repeated TEE during the study (eg, before another procedure or a control TEE for LA thrombus), this is also reported in the registry (separately for a given patient), together with data on the current antithrombotic treatment.

The primary endpoint of the study is the presence of LA thrombus on TEE.

The study was approved by the Ethics Committee of the Medical University of Warsaw (AKBE/113/2018). The Ethics Committee waived the requirement of obtaining informed consent from the patients.

Statistical analysis The proportion of patients undergoing ablation to those undergoing cardioversion, as well as patients' clinical characteristics and thromboembolic risk, may vary between participating centers depending on their individual profiles. Still, it may be anticipated that approximately 85% to 90% of enrolled patients will receive OAC. In OAC-treated populations, the prevalence of LA thrombus ranges from 1% to 10%.[8-12] If the registry includes a total of 2600 patients, over 100 cases of LA thrombus are anticipated, providing an adequate number of study endpoints for a logistic regression analysis of the predictors of LA thrombus. Receiver operating characteristic curves will be constructed and areas under the curve calculated to assess the prognostic accuracy of the CHA_2DS_2-VASc-RAF score (in comparison with other models) for the identification

TABLE 1 Laboratory data collected in the LATTEE registry

Test	Data
In all patients	
Blood tests	Complete blood count Creatinine, GFR Alanine and aspartate aminotransferases INR, APTT
TEE	Presence of LA thrombus Location of LA thrombus (LAA vs LA cavity) Presence of SEC, including dense SEC LAA emptying velocity (in relation to rhythm during TEE)
If available	
TEE	LAA morphology (windsock, chicken wing, cactus, or cauliflower)
Transthoracic echocardiography	Left ventricular ejection fraction (Ap4Ch/Ap2Ch) LA dimension (PLAX) LA area (Ap4Ch) LAVI (Ap4Ch/Ap2Ch)
Holter monitoring	Presence of AF or AFl AF or AFl burden

Abbreviations: AF, atrial fibrillation; AFl, atrial flutter; APTT, activated partial thromboplastin time; Ap2Ch, apical 2-chamber view; Ap4Ch, apical 4-chamber view; GFR, glomerular filtration rate; INR, international normalized ratio; LA, left atrial; LAA, left atrial appendage; LAVI, left atrial volume index; PLAX, parasternal long-axis view; SEC, spontaneous echo contrast; TEE, transesophageal echocardiography

of patients with LA thrombus. Analyses will be performed using the SAS software, version 9.2 (SAS Institute, Cary, North Carolina, United States).

Discussion The CHA_2DS_2-VASc score is a recommended tool for thromboembolic risk stratification in AF and AFl.[3] Still, it may not encompass all clinically relevant predictors of LA thrombus formation.[6,7,13-15] The type of AF has long been perceived as irrelevant for thromboembolic risk assessment. However, recently, nonparoxysmal AF has been shown to be independently associated with a higher risk of thromboembolic events than paroxysmal AF.[6,7,9] Moreover, in paroxysmal AF, evaluation of AF burden might improve thromboembolic risk stratification.[14] Renal dysfunction is another variable found to be a strong predictor of stroke and systemic embolism that is not included in the CHA_2DS_2-VASc score.[15]

Recently, a new CHA_2DS_2-VASc–based model, namely, the CHA_2DS_2-VASc-RAF score (R for renal dysfunction, AF for AF type), has proved superior to both the $CHADS_2$ and CHA_2DS_2-VASc scores in identifying patients with LA thrombus.[9] The primary goal of the LATTEE registry is to validate, and possibly recalibrate, the CHA_2DS_2-VASc-RAF score. Secondary analyses will include evaluation of LA thrombus risk in patients on different OAC regimens, depending on LA appendage (LAA) morphology, as well as in various predefined subgroups, including patients with heart failure, aortic stenosis, mitral regurgitation, diabetes, chronic kidney disease, men vs women, and elderly population.

The main limitation of the LATTEE registry is the use of a surrogate endpoint of LA thrombus and not ischemic stroke. However, LA thromboembolism represents the primary mechanism involved in the etiopathology of ischemic stroke in AF. Thus, we believe that the presence of LA thrombus on TEE may be considered an adequate surrogate endpoint. Another limitation, resulting from the study methodology (inclusion of patients referred for TEE), is that its participants—scheduled for ablation or cardioversion—can be expected to have lower thromboembolic risk than the general AF population. However, the identification of additional novel risk factors for LAA thrombus formation seems to be particularly valuable in patients with presumed low or intermediate thromboembolic risk (who will be adequately represented in the LATTEE registry) as opposed to those who are already known to be at high thromboembolic risk. Finally, it would be ideal to record all TEE studies and verify the presence of LA thrombus centrally in a core laboratory. However, this has not been undertaken in our registry.

In conclusion, the LATTEE registry is the largest study of patients with AF or AFl undergoing TEE in Poland. It will investigate the prognostic accuracy of the CHA_2DS_2-VASc-RAF score. It will also provide information on the residual risk of LA thrombus in patients treated with OAC and in different AF subpopulations. A significant number of centers participating in the LATTEE registry proves the utility of the "Club 30" Scientific Platform and reflects the will for integration of the young Polish scientific community.

ARTICLE INFORMATION

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CONFLICT OF INTEREST None declared.

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