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# Long Term Antiarrhythmic Effects of Thrombolytic Therapy in Pulmonary Embolism

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Background	The role of thrombolytic therapy in acute pulmonary embolism patients is still controversial considering the occurrence of arrhythmias. Short-term effects of thrombolytics are well-known whereas long-term effects on cardiac electrophysiology have not been reported before. The objective of our study was to assess the arrhythmic differences in pulmonary embolism patients who received thrombolytics followed by anticoagulation or anticoagulation alone.
Methods	Sixty patients who received thrombolytic therapy followed by anticoagulation (group 1) and 60 patients who received anticoagulation alone (group 2) were included in this retrospective, single-centre observational study. Twenty-four-hour ambulatory electrocardiography was performed $31 \pm 9$ months after pulmonary embolism hospitalisation in order to compare arrhythmias originating from both ventricles and atriums.
Results	The age and gender distribution of the patients were statistically similar. Ventricular arrhythmias were found to be same between t-PA and non t-PA groups. All types of atrial arrhythmias were found to be increased in non t-PA group even though left and right atrial volume indexes were statistically identical between the two groups.
Conclusion	In long-term pulmonary embolism, follow-up thrombolytic therapy was demonstrated to have atrial anti- arrhythmic effects.
Keywords	Pulmonary embolism • Arrhythmia • Thrombolytic • Anticoagulation • Ambulatory electrocardiography

#### Introduction

Pulmonary embolism is a life-threatening disease; adjusted pulmonary embolism hospitalisation rate is 302/100,000 in United States, even higher in black patients [1]. The corresponding ratio is unknown in Europe whereas, regionally considered, pulmonary embolism incidence is 20.8/10,000

per year in Malmo [2]. Predisposition factors related to pulmonary embolism are age, prior venous thromboembolism, active cancer, diseases that cause long-term bed rest, thrombophilia, oral contraceptives and hormone replacement therapy. Sudden onset of dyspnoea and tachycardia should alert clinicians for pulmonary embolism after further diagnostic modalities. The majority of patients die because of a failure in

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prompt diagnosis rather than inappropriate treatment. Biochemical tests, electrocardiography and echocardiography are primary diagnostic tools after pulmonary embolism suspicion. Moreover, computed tomography pulmonary angiography has become the standard imaging modality for the diagnosis of pulmonary embolism [3].

Thrombolytic therapy followed by anticoagulation versus anticoagulation alone are the main treatment strategies for pulmonary embolism. As pulmonary embolism promotes arrhythmias originating from the right ventricle [4], treatment options are expected to palliate and suppress the arrhythmias occurring secondary to pulmonary embolism. Considering in-hospital monitoring after acute pulmonary embolism, transient electrocardiographic abnormalities such as S1Q3 pattern or new right bundle branch block were proved to reflect right ventricular overload and critical pulmonary embolism. [5] Moreover, no major in-hospital ventricular arrhythmias were reported in acute pulmonary embolism patients even in the case of cardiopulmonary arrest. [5] On the other hand, apart from the treatment, a high incidence of atrial fibrillation after acute pulmonary embolism was also reported. [6] Even the precise reason was not defined for high atrial fibrillation incidence after acute pulmonary embolism; it may be explained by mutual risk factors between atrial fibrillation and pulmonary embolism. [6] Long-term antiarrhythmic effects of thrombolytic therapy in pulmonary embolism patients have not been reported before. Therefore the aim of our study is to compare arrhythmias in patients who were administered thrombolytic therapy followed by anticoagulation after pulmonary embolism diagnosis (group 1) and patients who were administered anticoagulation therapy alone (group 2). The importance of our study is, for the first time moderate to high risk pulmonary embolism patients were compared according to therapy regimen on the basis of atrial and ventricular arrhythmias. Thus, long-term effects of thrombolytic therapy on cardiac electrophysiology were investigated through 24-hour ambulatory electrocardiography.

#### Material and Methods

Our study was conducted with 172 consecutive patients who were diagnosed with moderate or high risk acute pulmonary embolism and were admitted to the coronary intensive care unit between February 2013 and August 2014. To reveal the at least two-year long-term antiarrhythmic effects of thrombolytic therapy, 24-hour ambulatory electrocardiograms were performed in August 2016. Our cardiology team informed patients about the study and their informed consents were obtained. The Local Ethical Committee of our hospital approved the study protocol. Patients were retrospectively enrolled in our study whereas they underwent 24-hour ambulatory electrocardiography prospectively.

A total of 172 patients diagnosed with moderate or high risk acute pulmonary embolism were included in our study (Figure 1). Patients who had atrial fibrillation on diagnosis

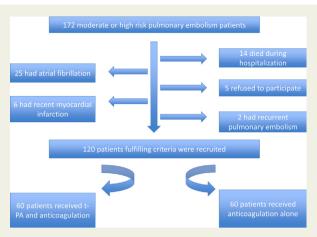


Figure 1 Patient recruitment and description for the study.

and developed atrial fibrillation during the follow-up period were excluded from the study. Patients with decreased ejection fraction, <35%, or patients who were diagnosed with acute coronary syndrome, recurrent pulmonary embolism or multi organ failure during the six months of the follow-up period were also excluded from the study in order to prevent the arrhythmic effect of ischaemia on atria and ventricles. Patients who were not contacted either by phone or who had no consent to re-admit to hospital were excluded. Fifty-two patients were excluded from the study, 25 of them had atrial fibrillation, 6 of them recently experienced myocardial infarction, 14 of them died during hospitalisation, 5 of them refused to participate, 2 of them had recurrent pulmonary embolism. Finally, 120 patients who fulfilled the criteria were recruited in the study. Sixty patients who received thrombolytic therapy (recombinant human plasminogen activatoralteplase-t-PA) followed by anticoagulation (group 1) and 60 patients who treated with anticoagulation alone (group 2) were included in the final study population. Two vials of alteplase (Actilyse 50 mg) were administered to group 1 in the two hours following the establishment of acute pulmonary embolism diagnosis according to guidelines [7]. Both groups received enoxaparin 1 mg/kg twice a day additional to warfarin treatment during the hospitalisation period. All of the patients enrolled in the study received anticoagulation with warfarin at least six months after the hospitalisation period. Patients underwent 24-hour ambulatory electrocardiography  $31 \pm 9$  months after pulmonary embolism hospitalisation.

#### **Analysis of Patient Data**

A clinical history of risk factors, such as age, sex, hypertension, diabetes mellitus, hyperlipidaemia, chronic lung and kidney disease was obtained from the hospital's medical database. Echocardiographic and pulmonary CT angiography data were also determined from the same database. Echocardiography was performed using a Vivid 7 system (GE Vingmed Ultrasound AS, Horten, Norway) in all patients in the first 48 hours during the coronary care unit

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