ORIGINAL ARTICLE

# Prediction of pulmonary embolism and its complication in diabetes mellitus type 2: a 5-year retrospective study

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## ABSTRACT

**Aim** To investigate the association between type 2 diabetes mellitus (T2DM) and pulmonary embolism, as well as to determine the prognostic value of troponin, D-dimer, prothrombotic, and proinflammatory markers in patients with T2DM.

**Methods** The retrospective cohort study included 305 patients with pulmonary embolism, divided into two groups: the first group with type 2 diabetes mellitus (n=165) and the control group without type 2 diabetes mellitus (n=140). Data were collected from May 2018 to May 2023. In all patients the following parameters were analysed: anthropometric parameters, laboratory parameters (troponin, D-dimer, CRP, fibrinogen, uric acid, glucose, total cholesterol, HDL cholesterol, LDL cholesterol, triglycerides), arterial blood pressure, antiphospholipid antibodies, HOMA-IR index, CT angiography of the pulmonary artery, rate of adverse clinical events in pulmonary embolism (need for inotropic catecholamine support, fibrinolysis, cardiopulmonary resuscitation) and the rate of intrahospital mortality from pulmonary embolism.

**Results** Patients with T2DM had elevated troponin, D-dimer, CRP, uric acid, fibrinogen, HOMA-IR and more severe clinical complications with higher mortality rates within 10 days of hospital admission. Significant predictors of PE in T2DM patients were found. Patients with pulmonary embolism in T2DM had a 4.38 times higher chance of death compared to patients with pulmonary embolism without T2DM.

**Conclusions** Troponin, D-dimer, prothrombotic, and proinflammatory markers have good prognostic value for short-term outcomes in PE among patients with T2DM.

**Key words:** D-dimer, proinflammatory markers, prothrombotic markers, troponin

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## INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a prothrombotic, proinflammatory, and hypofibrinolytic state (1), but the association between T2DM and pulmonary embolism (PE) is still unclear (2).

Pulmonary embolism is one of the most frequent cardiovascular diseases, with a high risk of adverse clinical outcomes (3). A significant number of patients at increased risk of pulmonary embolism is still not recognized in routine clinical practice (4).

The mechanisms of pulmonary embolism in patients with T2DM have not been fully understood, and they are still based on retrospective analysis of small databases (5-8). Several studies (8-10) have demonstrated that increased accumulation of adipose tissue and consecutive dysregulation of adipokine secretion precipitate a prothrombotic and proinflammatory state, resulting in vascular remodelling, atherosclerosis, and atherothrombosis. It seems that T2DM has a great potential to induce pulmonary embolism due to its procoagulant and hypofibrinolytic activity, but data exploring the role of T2DM in venous thromboembolism (VTE) are limited (11).

T2DM is a cluster of metabolic disorders, and next to hyperglycaemia and insulin resistance, co-existing changes like hypoglycaemia, obesity and dyslipidaemia also contribute to the prothrombotic state of patients with T2DM (12). In 2017, the International Diabetes Federation estimated that 451 million adults are diagnosed with diabetes mellitus worldwide, and the number would increase to 693 million by 2045 (13). In patients with diabetes, metabolic disorders disturb the physiological balance of coagulation and fibrinolysis, leading to a prothrombotic state characterized by platelet hypersensitivity, coagulation disorders and hypofibrinolysis (12).

Pulmonary embolism is often associated with severe clinical complications, such as right ventricular dysfunction and hemodynamic shock, which require prolonged hospitalization in intensive care units and optimal prognostic stratification is crucial for a good outcome and less frequent complications (14).

Type 2 diabetes mellitus promotes endothelial dysfunction and atherosclerosis (15). Therefore, the prothrombotic and proinflammatory markers of atherosclerosis may be used as predictors of pulmonary embolism and its complications in type 2 diabetes mellitus (12).

Diabetes mellitus type 2 with cardiovascular complications represents one of the most frequent health problems globally (16), but there is no major research of this type that could explain the relationship between pulmonary embolism and T2DM and offer an optimal combination of biomarkers for diagnosis and risk stratification of pulmonary embolism in T2DM, adapted to our health system.

Although underlying mechanism of T2DM is not clearly understood, in obese patients, impaired fibrinolytic activity has been consistently reported, and might be an important mechanism predisposing to both venous and arterial thrombosis (17-19). Whether this hypercoagulable state predisposes patients to pulmonary embolism is unknown.

The role of troponin in patients with acute pulmonary embolism has been widely investigated, but many questions remain open. Most authors agree that the role of troponin, similar to echocardiography, is primarily prognostic due to the low sensitivity and specificity in the diagnosis, but that elevated troponin values may indicate a group of patients with an increased risk of adverse outcomes (2).

In previous studies, plasma troponin values significantly correlated with the severity of the disease, i.e., right ventricular dysfunction (20-21). The basic approach to a patient with pulmonary embolism includes, in addition to a correct diagnosis, an accurate risk assessment that is the basis for further treatment (22).

Treatment of venous thromboembolism, including pulmonary embolism, requires enormous financial resources and compromises patients' quality of life (23).

Pulmonary embolism is responsible for almost all deaths in venous thromboembolism, but the association between type 2 diabetes mellitus and pulmonary embolism mortality is still not well understood (24). An improved understanding of the role that T2DM plays in pulmonary embolism could better inform clinicians on the most appropriate management of these patients, including the potential benefit of the initiation of adjuvant therapies aimed at the reduction of T2DM components, if they indeed are demonstrated to increase the risk of pulmonary embolism (1).

The aim of this study was to determine the prognostic value of troponin, D-dimer, prothrombotic, and proinflammatory markers for pulmonary embolism and its complications in patients with type 2 diabetes mellitus. Similar studies have not been conducted in our region yet.

## PATIENTS AND METHODS

### Patients and study design

This retrospective cohort study included the data of 305 patients with pulmonary embolism collected from May 2018 to May 2023 in the Department of Pulmonary Diseases at the University Clinical Centre Tuzla, divided into two groups: the first group with T2DM (n=165) and the control group the patients without T2DM (n=140). The inclusion criteria for the study entailed patients: with the first episode of pulmonary embolism confirmed by the computed tomography pulmonary angiogram (CTPA/CTPE), over 18 years of age, who had relevant laboratory parameters recorded, and patients who did not smoke. The research was conducted on adult patients (years range from 22-93 years). The exclusion criteria were: acute myocardial infarction, chronic heart failure, patients who had percutaneous transluminal coronary angioplasty (PTCA) and coronary artery bypass graft (CABG) surgery, acute infectious diseases, septic conditions, pneumonia, stroke, peripheral arterial disease, chronic kidney disease, liver disease, malignancy, gout, systemic connective tissue diseases, hormone replacement therapy, use of oral contraceptives and medications that could affect the lipid profile. Complications were registered as adverse clinical events in pulmonary embolism: need for inotropic catecholamine support, fibrinolysis, cardiopulmonary resuscitation and in-hospital death within 10 days of hospital admission. Conventional risk factors, use of drugs (statins, ACE inhibitors), level of physical activity, cardiovascular diseases, dietary habits and alcohol consumption were registered according to data obtained auto- and hetero-anamnestically.

This study was approved by the University Clinical Centre Tuzla review board. An informed consent was obtained from all patients.

### Methods

Pulmonary embolism was confirmed by the computed tomography pulmonary angiogram (CTPA/CTPE). Type 2 diabetes mellitus was diagnosed according to the criteria of the American Diabetes Association (25). Hospital records of both pulmonary embolism patients, with and without T2DM were retrospectively evaluated. Since all patients had undergone laboratory and CT diagnostics in hospital conditions, the hospital's database as a primary data source was used. In all patients with pulmonary embolism, the following was analysed: medical history and physical exam, anthropometric parameters (age, gender, body weight, body height, body mass index - BMI, waist circumference), laboratory parameters (troponin, D-dimer, C-reactive protein - CRP, fibrinogen, uric acid, fasting plasma glucose, total serum cholesterol, serum high-density lipoprotein - HDL cholesterol, serum low-density lipoprotein - LDL cholesterol, serum triglycerides), systolic and diastolic arterial blood pressure, antiphospholipid antibodies (APA), Homeostatic Model Assessment for Insulin Resistance (HOMA-IR) index, CT angiography of the pulmonary artery with 3D reconstruction, rate of adverse clinical events in pulmonary embolism (need for inotropic catecholamine support, fibrinolysis, cardiopulmonary resuscitation) and rate of intrahospital mortality from pulmonary embolism (in-hospital death within 10 days of hospital admission).

Body weight (kilogram - kg) was measured on a lever scale (Seca, GmbH & Co, Germany). Patients were weighed barefoot and lightly clothed. The obtained values were reduced by 0.9 kg, i.e. for the remaining clothing. Body height (centimetres - cm) was measured with a metal tape accurately calibrated and attached to the corresponding stand of the scale. Patients were measured in the "Frankfurt horizontal", where the top of the eyebrow was level with the top of the ear. Body mass index (BMI) ($kg/m^2$) was calculated according to the formula: weight (kg) / $[height\ (m)]^2$. Waist circumference (WCI) (in cm) was measured in the area of the navel and the fifth lumbar vertebra, with a regular tape measure. Biochemical parameters and D-dimer were performed at the Polyclinic for Laboratory Diagnostics of the Department of Biochemistry and Transfusion Polyclinic, Tuzla. Fasting plasma glucose (PGN)

(range 4.1-5.9 mmol/L) was determined by the enzyme-colorimetric method with hexokinase (Dimension RxL Max, Siemens, Germany).

Troponin (range 0.0-15.6 pg/mL for females and 0.0-34.2 pg/mL for males) was determined by the chemiluminescent microparticle immunoassay (Architect ci8200, Abbott, USA). D-dimer (range 0.0-0.55 mg/L) was determined by the quantitative immunoturbidimetric method (Innovance BCS, Siemens, Germany). Fibrinogen (range 1.8-3.5 g/L) was determined by the photo-optical method (BFT II, Siemens, Germany). CRP (range 0.0-3.3 mg/L), uric acid (UA) (range 155-357 μmol/L for females and 208 to 428 μmol/L for males), total cholesterol in serum (range 3.1-5.2 mmol/L), HDL cholesterol in serum (range 1.04-1.55 mmol/L), LDL cholesterol in serum (range 2.59-3.30 mmol/L), and triglycerides in serum (range 0.34-1.7 mmol/L) were determined by the enzymatic method (Dimension RxL Max, Siemens, Germany). Arterial blood pressure (in mm Hg) was measured with a manual sphygmomanometer (Bokang Instruments, China) in a sitting position, after resting for ten minutes. Arterial hypertension was considered at a value ≥135 mm Hg for systolic and ≥85 mm Hg for diastolic arterial blood pressure, as well as previously diagnosed and/or treated arterial hypertension. Antiphospholipid and/or anticardiolipin antibodies were determined by the enzyme-linked immunosorbent assay (Euroimmun, Germany). The HOMA-IR index (reference value <2.7 ) was calculated using the formula: HOMA IR= insulin in the blood (μU/mL) x fasting glucose in the plasma (mmol/L)/22.5.

### Statistical analysis

Descriptive statistics were employed to summarize the data, including measures of central tendency (mean) and measures of dispersion (standard deviation - SD). The significance of differences between samples was assessed using both parametric and nonparametric tests, depending on the nature of the data. Continuous data were presented as means ± standard deviation (SD) and were compared using an unpaired Student's t-test. The t-test was used for comparing continuous variables such as age, weight, height, BMI, waist circumference, glucose, CHOL, HDL, LDL, TGL, systolic blood pressure, diastolic blood pressure, troponin, D-dimer, CRP, uric acid, fibrinogen, and HOMA-IR. Categorical variables were reported as frequencies (%) and were compared using the $\chi 2$ test. Gender distribution, antiphospholipid antibodies (APA), inotropic support, fibrinolysis, cardiopulmonary resuscitation (CPR) and death status were analysed using the $\chi 2$ test. Statistical hypotheses were tested at a significance level ($\alpha$) of 0.05. Differences between the samples were considered statistically significant if $p< 0.05$. Additionally, logistic regression analysis was performed to assess the predictors of pulmonary embolism (PE) in T2DM patients, and to determine strength of the association between the model composed of two independent variables and the dependent variable. Dependent variable was a dichotomous (binary) variable, coded 0 or 1.

Contingency analysis test ($\chi^2$) was used to check whether two categorical variables were independent or not. The standard error (S.E.) was used for testing whether the parameter was significantly different from 0; by dividing the parameter estimate by the standard error a t-value was obtained. Beta coefficient (B) was used for direct comparisons between independent variables to determine which one had the most influence on the dependent variable. The degrees of freedom refer to the number of independent variables in regression model. If Exp(B) >1, then odds ratio = Exp(B). The Wald test was used to confirm whether a set of independent variables were collectively significant for a model or not. Significance for the model was tested at a significance level $p< 0.05$. Cox & Snell and Negelkerke coefficients of determination were used to predict the presence of pulmonary embolism in T2DM and for predicting influence of the predictors: type 2 diabetes mellitus, D-dimer and troponin on mortality in patients with pulmonary embolism.

## RESULTS

At the end of the study, the database consisted of the total of 6830 patients. Pulmonary embolism was confirmed in 305 patients who met the inclusion criteria. There were 152 males (49.84%) and 153 females (50.16%) (Table 1).

The mean age of the patients without T2DM was 60.6±17.64 years and 72.29±13.35 years for the patients with T2DM. The total number

**Table 1. Clinical characteristics of patients with pulmonary embolism (PE) in patients with and without diabetes mellitus type 2 (T2DM)**

| Variable | PE without T2DM (N=140) | PE with T2DM (N=165) | p |
|---|---|---|---|
| Mean age ±SD (years) | 60.6±17.64 | 72.29±13.35 | 0.62 |
| Male/female (No) | 85/55 | 67/98 | 0.63 |
| Obesity (No) | 5 | 165 | p<0.001 |
| Hypertension (No) | 2 | 143 | p<0.001 |
| Hypercholesterolaemia (No) | 9 | 86 | p<0.001 |
| Body weight (kg) | 70.02 | 92.14 | p<0.001 |
| Body height (cm) | 169.06 | 175.57 | p<0.001 |
| BMI | 22.7 | 32.2 | p<0.001 |
| Waist circumference (cm) | 81.18 | 115.5 | p<0.001 |
| Total cholesterol (mmol/L) | 4.38 | 5.33 | p<0.001 |
| HDL cholesterol (mmol/L) | 1.19 | 0.89 | p<0.001 |
| LDL cholesterol (mmol/L) | 3.11 | 4.3 | p<0.001 |
| Triglycerides (mmol/L) | 2.04 | 3.99 | p<0.001 |
| Glucose (mmol/L) | 4.74 | 8.58 | p<0.001 |
| C-reactive protein (mg/L) | 33.56 | 115.93 | p<0.001 |
| Uric acid (μmol/L) | 295 | 404.5 | p<0.001 |
| Fibrinogen (g/L) | 3.26 | 4.71 | p<0.001 |
| Systolic blood pressure (mmHg) | 114.82 | 147.81 | p<0.001 |
| Diastolic blood pressure (mmHg) | 75.82 | 94.51 | p<0.001 |
| HOMA-IR | 1.33 | 3.18 | p<0.001 |
| Antiphospholipid antibodies (%) | 0 | 12 | p<0.001 |

BMI, body mass index; CHOL, total serum cholesterol; LDL, low-density lipoprotein; HDL, high-density lipoprotein; CRP, C-reactive protein; HOMA-IR, Homeostatic Model Assessment for Insulin Resistance

of patients in the group with pulmonary embolism with T2DM was 165, 67 (40.61%) males and 98 (59.39%) females. The total number of patients in the group with pulmonary embolism without T2DM was 140, 85 (60.71%) males and 55 (39.29%) females (p=0.63). The patients with pulmonary embolism in the T2DM group significantly more frequently had hypertension, obesity and hypercholesterolaemia compared with the controls (p<0.001), a significantly higher waist circumference than in the patients with pulmonary embolism without T2DM (115.5 vs. 81.18 cm; p<0.001). There was a statistically significant difference in body mass index (BMI) between the patients with pulmonary embolism with T2DM compared with the controls (p<0.001). Total cholesterol (5.33 vs. 4.38 mmol/L; p<0.001), LDL cholesterol (4.3 vs. 3.11 mmol/L; p<0.001), and triglycerides (3.99 vs. 2.04 mml/L; p< 0.001) were significantly higher in patients with pulmonary embolism in T2DM group, compared with the control group. HDL cholesterol (0.89 vs. 1.19 mmol/L; p<0.001) was significantly lower in patients with pulmonary embolism in the T2DM group, compared with the control group.

Mean glucose values (8.59 vs. 4.74 mmol/L; p<0.001), CRP (115.93 vs. 33.56 mg/L; p<0.001), fibrinogen (4.71 vs. 3.26 g/L; p<0.001), and uric acid (404.5 vs. 295 μmol/ L; p<0.001) were significantly higher in patients with pulmonary embolism in the T2DM group, compared with the control group. Patients with pulmonary embolism in T2DM group significantly more frequently had higher systolic (147.81 vs. 114.82 mm Hg; p<0.001), diastolic blood pressure (94.51 vs. 75.82 mm Hg; p<0.001), HOMA-IR (3.18 vs. 1.33; p<0.001), and more frequent antiphospholipid antibodies (p<0.001) compared with the controls (Table 1).

The serum troponin values (148.17 pg/mL vs. 7.07 pg/mL; p<0.001), D-dimer (4.44 mg/L vs. 3.60 mg/L; p<0.001) were significantly higher in patients with pulmonary embolism in the T2DM group, compared with the control group. Intermediate-risk pulmonary embolism (p<0.001) and high-risk pulmonary embolism (p<0.001) were more frequent in patients with pulmonary embolism in the T2DM group, compared with the control group. There was no significant difference regarding low risk pulmonary embolism between the patients with T2DM and without T2DM (p>0.53). Patients with pulmonary embolism in T2DM proved to have significantly more clinical complications: a need for inotropic catecholamine support (p<0.001), fibrinolysis (p<0.001), cardiopulmonary resuscitation (p<0.001), and in-hospital death within 10 days of hospital admission (p<0.001), compared to patients without T2DM (Table 2).

**Table 2. Characteristics of pulmonary embolism and its complications in patients with pulmonary embolism (PE) in patients with and without diabetes mellitus type 2 (T2DM)**

| Variable | PE without T2DM (N=140) | PE with T2DM (N=165) | p |
|---|---|---|---|
| Troponin (pg/mL) | 7.07 | 148.17 | p<0.001 |
| D-dimer (mg/L) | 3.60 | 4.40 | p<0.001 |
| **Complications** (No of patients) | | | |
| High-risk PE | 2 | 6 | p<0.001 |
| Intermediate-risk PE | 17 | 43 | p<0.001 |
| Low-risk PE | 121 | 116 | p>0.53 |
| Inotropic catecholamine support | 4 | 15 | p<0.001 |
| Fibrinolysis | 2 | 6 | p<0.001 |
| Cardiopulmonary resuscitation | 1 | 8 | p<0.001 |
| Intrahospital mortality | 4 | 18 | p<0.001 |

Logistic regression model for predicting the presence of pulmonary embolism in the T2DM group showed statistical significance (p<0.001). Patients with T2DM and pulmonary embolism had 39 time greater chance to have elevated tro-

ponin and 45 times greater chance to have elevated D-dimer when compared to PE patients without T2DM. According to the values of the Cox & Snell and Negelkerke coefficients of determination, the model explains between 42.7% and 57.10% of the variance in the presence of T2DM in patients with pulmonary embolism. Elevated values of troponin and D-dimer were statistically significant (=169.91; p<0.001) in the prediction of the presence of pulmonary embolism in type 2 diabetes mellitus (Table 3).

**Table 3. Influence of troponin and D-dimer predictors on pulmonary embolism in type 2 diabetes mellitus**

| Variable | B | S.E | Wald | Df | Significance | Exp (B) |
|---|---|---|---|---|---|---|
| hs-Troponin | 3.66 | 0.36 | 105.24 | 1.00 | 0.00 | 39.00 |
| D-dimer | 19.92 | 28420.70 | 0.00 | 1.00 | 1.00 | 44.87 |
| Constant | -21.20 | 28420.70 | 0.00 | 1.00 | 1.00 | 0.00 |
| $\chi 2$ for model | 169.91 | | | | | |
| df (degrees of freedom) for model | 2 | | | | | |
| Significance for model | 0.00 | | | | | |
| Cox & Snell | 0.427 | | | | | |
| Nagelkerke | 0.571 | | | | | |

B, beta coefficient; S. E., standard errors; Wald, Wald $\chi 2$ test; Df, degrees of freedom for the model; significance, significance, F for model; Exp (B), odds ratio; constant, the value at which the regression line crosses the y-axis)

Logistic regression model for predicting the influence of the type 2 diabetes mellitus predictors, D-dimer and troponin on mortality in patients with pulmonary embolism showed statistical significance (p<0.001). The death prediction model showed statistical significance (=32.36; p<0.001). According to the values of the Cox & Snell and Negelkerke coefficients of determination, the model explained between 10.10% and 23.80% of the variance of the fatal outcome (Table 4).

Logistic regression results showed that patients with elevated troponin values were 13.18 times more likely to die from pulmonary embolism, while patients with elevated D-dimer values were 58.43 times more likely to die from pulmonary embolism in the T2DM group. Patients with pulmonary embolism with T2DM had a 4.38 times higher chance of death compared to patients with pulmonary embolism without T2DM. Elevated values of troponin and D-dimer were statistically significant (p<0.001) in the prediction of death, as well as the presence of T2DM in patients with pulmonary embolism (Table 4).

**Table 4. Influence of troponin and D-dimer predictors on pulmonary embolism mortality in type 2 diabetes mellitus**

| Variables | B | S.E | Wald | Df | Significance | Exp (B) |
|---|---|---|---|---|---|---|
| hs-Troponin | 2.58 | 1.14 | 5.08 | 1.00 | 0.024 | 13.18 |
| D-dimer | 15.58 | 28420.70 | 0.00 | 1.00 | 1.000 | 58.43 |
| Type 2 diabetes mellitus | 1.48 | 1.15 | 1.64 | 1.00 | 0.200 | 4.38 |
| Constant | -21.20 | 28420.70 | 0.00 | 1.00 | 0.999 | 0.00 |
| $\chi 2$ for model | 32.36 | | | | | |
| df (degrees of freedom) for model | 3 | | | | | |
| Significance for model | 0.00 | | | | | |
| Cox & Snell | 0.101 | | | | | |
| Nagelkerke | 0.238 | | | | | |

B, beta coefficient; S. E., standard errors; Wald, Wald $\chi 2$ test; Df, degrees of freedom for the model; significance, significance, F for model; Exp (B), odds ratio; constant, the value at which the regression line crosses the y-axis;

## DISCUSSION

Our study provides important insights into the stratification of pulmonary embolism patients, based on type 2 diabetes mellitus status and mortality outcomes. The results indicate several significant associations and highlight potential risk factors for these patient populations.

Type 2 diabetes mellitus is a generalized thromboembolic disease. Many studies highlight the importance of routine detection of elevated prothrombotic and proinflammatory markers in T2DM because of the higher cardiovascular risk (26,27). In this study, prothrombotic and proinflammatory markers in T2DM were significantly higher in patients with pulmonary embolism with T2DM compared to the patients with pulmonary embolism without T2DM. Prognostic stratification of patients with pulmonary embolism with T2DM is very important in the treatment and potential improvement of clinical outcomes (28).

According to the results of this study, patients with pulmonary embolism with T2DM had a significantly higher waist circumference and BMI. In a study by Ray et al. (29) and Steffen et al. (30), an increase in BMI above the normal value was associated with an increase risk of venous thromboembolism (VTE), which is similar with our results.

The current analyses suggest a strong indication for a wide assessment of metabolic anomalies and the need for a multidisciplinary approach to the patients with T2DM and its comorbidities (27).

In this research, patients with pulmonary embolism with T2DM had significantly higher values of total cholesterol, LDL cholesterol, triglycerides,

and glucose and lower values of HDL cholesterol compared to the patients without T2DM, which is in contrast with some other studies in which total serum cholesterol was not significantly different between patients with pulmonary embolism and controls (29). In a study by Ageno (5), hypercholesterolemia and low HDL cholesterol were linked to an increased risk of VTE, which is in accordance with our results. In a study by Wang et al. (31), there was a negative correlation between pulmonary embolism and HDL cholesterol values, with a trend of decreasing HDL cholesterol in patients with PE, which is consistent with the results of our research. In a study by Ray et al. (29), patients with elevated fasting glucose had a high incidence of pulmonary embolism, which is in accordance with our results.

Fibrinogen increases plasma viscosity and platelet aggregation (32). Our results showed that patients with pulmonary embolism with T2DM had significantly higher CRP values, fibrinogen, and uric acid, which is consistent with the results of the previous studies (29, 33-34), indicating that fibrinogen, CRP and uric acid could play an important role in defining the severity of T2DM and potential complications, including pulmonary embolism.

In this study patients with pulmonary embolism in T2DM had significantly higher values of troponin and D-dimer compared to patients without T2DM. High elevation of troponin in patients with pulmonary embolism was reported in some studies (35), which is consistent with the results of our study; however, there is also a report with low prevalence (36).

Our research found that troponin and D-dimer were significant predictors of pulmonary embolism in type 2 diabetes mellitus; patients with elevated troponin values and T2DM have 39 times greater chance to have elevated troponin, and 45 times greater chance to have elevated D-dimer when compared to PE patients without type 2 diabetes mellitus. Other studies also showed elevated troponins as good predictors of a possible bad outcome in acute pulmonary embolism (37), which is in accordance with the results of our study. Our results showed that measuring troponin values in patients with pulmonary embolism with T2DM could potentially separate patients with high and intermediate-risk of pulmonary embolism from patients with low-risk, and troponin could potentially be used for risk assessment and early detection of PE in this population, which is consistent with the results of the previous studies (37).

To the best of our knowledge, we are the first to report findings that patients with pulmonary embolism in T2DM have 4.38 times higher chance of death compared to the patients without T2DM.

The results of our study have important clinical implications, confirming that troponin has great prognostic power. Measuring troponin values allows indirect assessment of right ventricular status in patients with pulmonary embolism in the patients with T2DM and helps to make a decision which patients can be safely returned to outpatient treatment and which patients must be treated in hospital conditions. Also, this research enables the selection of high-risk patients with pulmonary embolism with T2DM, who can develop more severe complications and require hospitalization in intensive care units.

Our study enhances the understanding of the relationship between T2DM, PE, and mortality outcomes, providing valuable insights for risk assessment and management strategies in this patient population. The findings emphasize the importance of considering clinical indicators, biomarkers, and comorbidities to identify T2DM patients at higher risk for adverse events. Further research is warranted to validate these findings, explore potential therapeutic interventions, and develop personalized approaches to improve patient outcomes in this complex population. These assessments can very easily be added to the standard clinical risk assessment procedures and be of significant value in future secondary prevention planning.

There are two major limitations in this study that could be addressed in future research: it was based on a relatively small cohort from a single centre and the study focused exclusively on laboratory markers, since we did not have the possibility of ultrasound assessment of right ventricular dysfunction, and the second one is a relatively small sample size.

In conclusion, troponin, D-dimer, prothrombotic and proinflammatory marker levels may be used as additional prognostic markers of pulmonary embolism and its complications in patients with type 2 diabetes mellitus for short-term outcomes. De-

termination of troponin, D-dimer prothrombotic and proinflammatory marker levels at admission to the hospital may help create a better risk stratification for patients with pulmonary embolism and type 2 diabetes mellitus. The presence of T2DM in patients with pulmonary embolism is associated with significantly higher rates of complications and mortality, and the right identification of these risk factors is necessary to reduce the risk.

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## TRANSPARENCY DECLARATION

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