DIAGNOSIS OF PULMONARY EMBOLISM IN THE EMERGENCY DEPARTMENT

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SUMMARY – The aim of this study was to determine the association of clinical presentation, the Wells scoring system and D-dimer values with MSCT pulmonary angiography. A case control study was conducted in the Emergency Department of the Clinical Hospital Sveti Duh throughout 2019. Patients with a referral diagnosis of a pulmonary embolism were included in the study. Patients were divided into two groups. The first group consisted of patients diagnosed with pulmonary embolism by MSCT pulmonary angiography or *postmortem*, and the second group consisted of patients excluded from pulmonary embolisms. For the Wells score, D-dimers, troponin, respiratory rate and peripheral blood oxygen saturation, statistically significant differences were found between groups of patients with confirmed or excluded pulmonary embolism (p <0.001). For heart rate, chest pain, syncope, and hemoptysis, no statistically significant differences were found between these two groups of patients. Deep venous thrombosis of the lower extremities was found by ultrasound in > 70% of patients with massive a pulmonary embolism. Pulmonary embolism was confirmed in all patients for whom a high risk was calculated according to the Wells score. In conclusion, a low degree of clinical probability (according to the Wells score), along with a normal concentration of D-dimer, are a sure strategy in excluding pulmonary embolism.

Keywords: pulmonary embolism, Wells score, D-dimers, MSCT pulmonary angiography, emergency medical service

Introduction

Venous thromboembolism is a clinical entity that includes deep vein thrombosis (DVT) and pulmonary embolism (PE). Pulmonary embolism is an emergency caused by sudden obstruction of the pulmonary circulation by a blood clot. It represents a serious diagnostic - therapeutic challenge in emergency and intensive care units. It is the third most common cardiovascular disease with an estimated incidence of 100 - 200: 100.000 inhabitants.^{1,2} Thromboembolus most com-

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monly originates from the veins of the lower extremities and pelvis. A thrombus forms in a vein, and when mobilized it travels through the venous system and the right heart and reaches the pulmonary arteries, where it partially or completely clogs one or more branches. The clinical presentation depends on the degree of involvement of the pulmonary circulation, and patients are most often presented with dyspnea, tachypnea, chest pain, fainting or complete loss of consciousness.^{3–5} PE may remain unrecognized and undiagnosed due to a nonspecific clinical presentation.⁶ In addition to the anamnesis and physical examination, which are most important in establishing clinical suspicion of PE, we also used the calculation of the Wells scoring system and the laboratory value of D-dimer. There are

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diagnostic algorithms that assess the risk of suspected pulmonary embolism and determine further diagnostic and therapeutic procedures. The final diagnosis is made by MSCT pulmonary angiography, which is the diagnostic gold standard. Ultrasound of the right heart and/or ultrasound detection of deep vein thrombosis in the veins of the lower limbs or pelvic veins also play an important role.^{7,8} Treatment is initiated by correction of hypoxemia and hypovolaemia and anticoagulant or thrombolytic therapy, depending on the clinical presentation of PE. If treatment is with anticoagulants, unfractionated or low-molecular-weight heparin and vitamin K antagonists or direct oral anticoagulants are most commonly used.

Subjects and methods

The study included patients with a pulmonary embolism, who were examined in the ED (Internal Medicine Clinic) of the Clinical Hospital Sveti Duh from January to the end of December 2019. A case control study was conducted and patients were divided into two groups based on the findings. After the anamnesis was taken and a physical examination conducted, the patients had an electrocardiogram, blood was taken for laboratory tests, and they were then sent for X-rays of the heart and lungs. Based on the clinical presentation, Wells scoring system, and elevated D-dimer values, PE was suspected in 305 patients. The final diagnosis of pulmonary embolism was confirmed by MSCT pulmonary angiography. Ultrasound diagnostics was performed with the aim of detecting deep venous thrombosis. The research was approved by the Ethics Committee of Clinical Hospital Sveti Duh.

Statistical methods

SAS 9.1 software, licensed for the University Computer Center (SRCE, site: 0082452005), was used in the analysis. Distributions of quantitative data analyzed for normality by the Smirnov-Kolmogorov test showed that the distribution is not normal, except for heart rate data. Therefore, nonparametric and parametric analytical procedures were used in the analysis for heart rate data (conventional measures of descriptive statistics and t-test). Distributions are described by standard measures of descriptive statistics (median (M) minimum (min) and maximum value (max) and interquartile range (IQR)). They were analyzed by the Kruskall-Wallis test. Distributions of qualitative data were analyzed by $\chi 2$ test and Fisher 's exact test. The results were interpreted at the 5% level of significance.

Results

During 2019, 22.252 patients were examined at the Emergency Department (internal medicine clinics) of the Clinical Hospital Sveti Duh; and 305 of them were suspected of having a pulmonary embolism. In 149 patients, a diagnosis of PE was made, which is a frequency of 0.7%. In the remaining 156 patients, the diagnosis of PE was ruled out. The majority of patients (> 80%) were over 60 years old. Approximately 60% of the patients were female.

For the Wells score, D-dimers, troponin and respiratory rate, statistically significant differences were found between the groups of patients who were confirmed or excluded from the diagnosis of PE (p < 0.001) (Table 1). Peripheral blood oxygen saturation was statistically significantly lower in the group of patients with confirmed PE (Table 2). Regarding heart rate, no statistically significant difference was found between the examined groups. The most significant risk factors for pulmonary embolism in our study were: immobilization (32.89%), malignancy (17.45%), major surgery (8.72%) and previous DVT / PE (5.37%). Deep venous thrombosis of the lower extremities was also

Table 1. Review of examined indicators and their statistical significance

| Indicators | confirmed PE | E excluded PE | |
|------------------|------------------------|------------------------|--------|
| | median (25th and 75th) | median (25th and 75th) | þ |
| Wells score | 5,5 (4,5-7) | 1,5 (0-2,5) | <0,001 |
| D-dimers | 4264 (4189-4327) | 4078 (1654-4327) | <0,001 |
| troponin | 60 (17-239) | 27 (10-104) | <0,001 |
| respiratory rate | 91 (86-95) | 94 (90-97) | <0,001 |

| | Pulmonary embolism | | |
|------------|--------------------|-------------|--|
| | Confirmed | Excluded | |
| chest pain | 72 (48,32%) | 65 (41,67%) | |
| syncope | 34 (22,82%) | 32 (20,51%) | |
| hemoptysis | 2 (1,34%) | 7 (4,49%) | |
| SpO2 < 90% | 72 (48,32 %) | 39 (25%) | |

Table 2. Distribution of examined clinical signs / symptoms

| Table 3. Incidence | of pulmonary | embolism | according to | 2 |
|--------------------|--------------|----------|--------------|---|
| Wells score | | | | |

| | | Proven pulmonary emboly | | |
|-------|------------|----------------------------|-----|-------|
| | Risk | Yes | No | Total |
| WELLS | <2 low | 3 | 117 | 120 |
| score | 2-6 medium | 108 | 39 | 147 |
| | >6 high | 38 | 0 | 38 |
| Total | | 149 | 156 | 305 |

found by ultrasound in > 70% of patients with massive pulmonary embolism. In all patients (100%) for whom a high risk was calculated according to the Wells score (> 6 points), PE was confirmed, while in 97.5% of patients who were excluded from the PE, the Wells score showed a low risk (<2 points). The differences found were statistically significant ($\chi 2$ (2) = 178.19, p <0.001; $\chi 2$ test) (Table 3). The odds ratio (OR) showed that patients with medium and high Wells scores were 47 times more likely to develop pulmonary embolism than the low score group, OR = 47.77, p <0.001 (95% CI: 22, 28, 102.44).

In 48.85% of patients (149/305) MSCT pulmonary angiography confirmed the diagnosis of PE, which is almost every second patient who is suspected of PE based on the clinical presentation, Wells score and D-dimer.

Discussion

The obtained results showed a frequency of PE of 0.7%, which corresponds to the literature data. A retrospective analysis based on several international databases found a prevalence of PE of less than 1%. According to Valle et al., the incidence of PE in the emergency department was 1.01 per 1,000 patients.⁹ In our study, > 80% of the patients were over 60 years

old and about 60% of them were women, while the results of the same authors show that the average age of respondents was 72 years, and 58% were women. As many as 72% of respondents were over 65 years old.^{9,10} Among the conclusions of the searched literature, it is stated that PE is more often diagnosed in women and elderly patients due to associated diseases and risk factors that increase with age. The calculation of the Wells scoring system and the value of D-dimer proved to be a good diagnostic strategy in the exclusion of PE. However, in our study, as evidenced by the literature, D-dimers did not prove effective in differentiating the severity of the clinical picture.¹¹ The group of authors states that the negative predictive value of D-dimer (<500 ng / ml) was 93.7%, and in combination with the Wells score (for risk \leq 4) 100%.^{12,13,14} According to Pasha et. al. the incidence of low-risk PE morbidity based on the Wells score and normal D-dimer concentration is 0.34% with a negative predictive value of 99.7%.^{14,15} The sensitivity of D-dimers is 95%, while their specificity is about 50%. MSCT pulmonary angiography is the diagnostic gold standard, with a sensitivity of 83% and a specificity of 96%.

According to the literature, the most common symptoms/signs of the disease were also dyspnea, chest pain and syncope. However, in our study syncope was a more frequent sign of suspected PE (20%: 9%). 9,15-17 According to Akbas et. al. the mean value of respiratory rate was 28/min, the mean value of blood oxygen saturation was 88% (without oxygen compensation), while the mean value of the heart rate was 88.5/min.¹⁸ For heart rate, no statistical significance was shown in our study in relation to the group of patients who were excluded from the diagnosis of PE. According to the literature consulted, dyspnea was present in more than 70% of patients in our study. Regarding risk factors, malignancy, immobilization, major surgery and previous PE were most often mentioned, which is evident from our research.

Thus, the diagnosis of PE is often difficult due to non-specific clinical presentation and it is extremely important to set the initial suspicion of this disease in time. A detailed clinical examination and anamnesis, supplemented by the calculation of the Wells score and the laboratory value of D-dimer, can establish the clinical suspicion of PE.

Ultrasound also plays an important role in the early and rapid detection of patients with signs of shock.

In conclusion, low risk according to the Wells score together with normal D-dimer concentration is a reliable strategy in excluding pulmonary embolism.

References

- Heit JA. The epidemiology of venous thromboembolism in the community. Arterioscler Thromb Vasc Biol 2008;28(3): 370–372. 10.1161/ATVBAHA.108.162545
- 2. Cohen AT, Agnelli G, Anderson FA, Arcelus JI, Bergqvist D, Brecht JG et al. Venous thromboembolism (VTE) in Europe. The number of VTE events and associated morbidity and mortality. Thromb Haemost 2007;98(4):756–764.
- 3. Degoricija V. et al. Hitna medicina, Zagreb; Libar, 2013.
- 4. Gašparović V. et al. Hitna medicina, 2., dopunjeno i obnovljeno izdanje, Zagreb; Medicinska naklada, 2019.
- McIntyre KM, Sasahara AA. The hemodynamic response to pulmonary embolism in patients without prior cardiopulmonary disease. AmJCardiol 1971; 28(3): 288–294. 10.1016/0002-9149(71)90116-0
- Burrowes KS, Clark AR, Tawhai MH. Blood flow redistribution and ventilationperfusion mismatch during embolic pulmonary arterial occlusion. Pulm Circ 2011;1(3):365–376. 10.4103/2045-8932.87302
- Becattini C, Vedovati MC, Agnelli G. Prognostic value of troponins in acute pulmonary embolism: a meta-analysis. Circulation 2007; 116(4):427- 433. 10.1161/CIRCULATION-AHA.106.680421
- Jimenez D, Uresandi F, Otero R, Lobo JL, Monreal M, Marti D et al. Troponin-based risk stratification of patients with acute nonmassive pulmonary embolism: systematic review and metaanalysis. Chest 2009;136(4):974–982. 10.1378/chest.09-0608
- Valle HA, Ezguerra PG, Gonzalez IS, Martinez PH, Artacho PR, Hernandez SJ. Nonsuspected pulmonary embolism in the emergency department. Eur J Emerg Med 2020;27(5): 379–380. 10.1097/MEJ.000000000000683
- Sikora Skrabaka M, Skrabaka D, Ruggeri P, Caramori M, Skoczynski S, Barczyk A. D-dimer value in the diagnosis of

pulmonary embolism—may it exclude only? J Thorac Dis 2019; 11(3):664–672. 10.21037/jtd.2019.02.88

- Rubini G, Ferrari C, Cimino A, Fanelli M, Altini C, Gaudiano A et al. How often suspected pulmonary embolism is diagnosed and its main diagnostic characteristics, in an emergency nuclear medicine service? Four years experience. Hell J Nucl Med 2019;22(3):187–193. 10.1967/s002449911054
- Douma RA, Tan M, Schutgens R, Bates SM, Perrier A, Legnani C et al. Using an age-dependent D-dimer cut-off value increases the number of older patients in whom deep vein thrombosis can be safely excluded. Haematologica, 2012 Oct; 97(10):1507–13. 10.3324/haematol.2011.060657
- Guo DJ, Zhao C, Zou YD, Huang XH, Hu JM, Guo L. Values of the Wells and Revised Geneva Scores Combined with D-dimer in Diagnosing Elderly Pulmonary Embolism Patients. Chin Med J (Engl.) 2015;128(8):1052–1057. 10.4103/ 0366-6999.155085
- Pasha SM, Klok FA, Snoep JD, Mos ICM, Goekoop RJ, Rodger MA et al. Safety of excluding acute pulmonary embolism based on an unlikely clinical probability by the Wells rule and normal D-dimer concentration: A meta-analysis. Thromb Res. 2010;125(4):e123–e127. 10.1016/j.thromres.2009.11.009
- Badertscher P, de Lavallaz JF, Hammerer Lercher A, Nestelberger T, Zimmermann T, Geiger M et al. Prevalence of Pulmonary Embolism in Patients With Syncope. J Am Coll Cardiol. 2019;74(6):744-754. 10.1016/j.jacc.2019.06.020
- Tamburkovski V, Anđelić S. Wells' score for early prehospital screening of pulmonary embolism. Signa Vitae 2016;12(1): 131–133.
- Parent F, Maître S, Meyer G, Raherison C, Mal H, Lancar R et al. Diagnostic value of D-dimer in patients with suspected pulmonary embolism: Results from a multicentre outcome study. Thromb Res. 2007;120(2):195–200. 10.1016/j.thromres. 2006.09.012
- Akbas I, Kocak AO, Celik BK, Menekse TS, Demir M, Gur STA et al. Performance of integrated pulmonary index for pulmonary embolism in dyspneic patients. Bratisl Lek Listy. 2021; 122(1):65–70. 10.4149/BLL_2021_008

Sažetak

DIJAGNOSTIKA PLUĆNE EMBOLIJE U OBJEDINJENOM HITNOM BOLNIČKOM PRIJAMU

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Cilj rada je bio utvrditi povezanost kliničke slike, Wellsovog bodovnog sustava i vrijednosti D-dimera s MSCT plućnom angiografijom. Provedena je studija istraživanja parova u Objedinjenom hitnom bolničkom prijamu Kliničke bolnice "Sveti Duh" tijekom cijele 2019. godine. U istraživanje su bili uključeni bolesnici sa uputnom dijagnozom plućne embolije. Bolesnici su podijeljeni u dvije skupine. U prvoj su skupini bili bolesnici kojima je dijagnoza plućne embolije potvrđena MSCT plućnom angiografijom ili *post mortem*, a drugu skupinu su činili bolesnici kod kojih je isključena plućna embolija. Za Wellsov skor, D-dimere, troponin, frekvenciju disanja i perifernu zasićenost krvi kisikom nađene su statistički značajne razlike između skupina bolesnika s potvrđenom, odnosno isključenom plućnom embolijom (p<0,001). Za frekvenciju srca, bol u prsima, sinkopu i hemoptizu nije nađena statistički značajna razlika između ove dvije skupine bolesnika. U >70% bolesnika s masivnom plućnom embolijom ultrazvučno je nađena duboka venska tromboza donjih ekstremiteta. Kod svih bolesnika kojima je prema Wellsovom bodovnom skoru izračunat visok rizik potvrđena je plućna embolija. Zaključno, niski stupanj kliničke vjerojatnosti (prema Wellsovom bodovnom skoru) zajedno s normalnom koncentracijom D-dimera sigurna su strategija u isključenju plućne embolije.

Ključne riječi: plućna embolija, Wellsov skor, D-dimeri, MSCT plućna angiografija, hitna medicinska služba