

## Editorial

# The Diagnostic Challenge of Pulmonary Embolism in Elderly Patients: Shifting the Context behind the Emergency Department

**Malatino L\*, Corriere T and Di Marca S**

Department of Clinical and Experimental Medicine, Unit and Chair of Internal Medicine, Cannizzaro Hospital, University of Catania, Catania, Italy

**\*Corresponding author:** Lorenzo Malatino, Chairman of Internal Medicine, Chief Unit of Internal Medicine, University of Catania c/o Cannizzaro Hospital, Via Messina 829, 95126 Catania, Italy**Received:** August 30, 2016; **Accepted:** September 14, 2016; **Published:** September 16, 2016

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Pulmonary Embolism (PE) is a life-threatening disease state associated with a mortality rate of approximately 30 % that may cause sudden death within few hours [1-3]. Its clinical presentation is variable and nonspecific and may also be symptomless [4]. While symptoms and signs are highly variable in patients with PE [5-6], early diagnosis is fundamental, as immediate treatment is highly effective. The current diagnostic approach of patients with a suspected PE is based on the assessment of clinical pretest probability, using clinical prediction scores, and serum D-dimer measurement [7-8].

The most widely used clinical prediction tools are the Wells score and the revised Geneva score [7,9,10]. The Wells score has been extensively validated using both a three-category (low, moderate or high clinical probability) and a two-category (PE likely or unlikely) schemes [7]. The revised Geneva score is entirely based on clinical variables, thus providing a three-category scheme (low, intermediate, and high clinical probability) [9].

The performance of these scores, however, has so far mostly been tested in the Emergency Department and in populations with low prevalence of elderly patients. Although the American Academy of Family Physicians (AAFP) and the American College of Physicians (ACP) recommend the use of the Wells prediction score, the guideline underscores that the Wells system performs better in younger patients without comorbidities or history of venous thromboembolism, a clinical setting which is rarely observed in the Department of Internal Medicine where elderly patients with several comorbidities are the majority.

Thus, to date, the direct comparison between the Wells and the revised Geneva scores in elderly hospitalized patients has been little performed, whereas most studies in patients with suspected PE were carried out in an emergency department [11,12].

For these reasons, in our recent study, it was assessed the applicability of the guidelines for the diagnosis of PE comparing the diagnostic power for PE of Wells and revised Geneva scores in two independent cohorts of elderly patients with several co-morbidities,

hospitalized in a non-emergency department.

Our study demonstrated that the Wells score is superior to the revised Geneva score for the diagnosis of PE in a cohort of elderly patients hospitalized in our Department of Internal Medicine [13].

On the other hand, previous studies in younger patients recruited from emergency departments showed a similar performance of these two scoring systems [14,15], as also reported in a recent meta-analysis including 29 studies [10].

Similarly to our recent observation [13], a better performance of the Wells score was demonstrated in previous studies in younger patients, and in two small studies in a Chinese population [11,16-19]. In one of these studies [19] the greatest accuracy was shown by the Pisa score. However, the Pisa score is very difficult to be applied in clinical practice and it appears to be more suitable for research purposes.

The superiority of the Wells score observed in a cohort of elderly patients with several co-morbidities may be related to the high mean age, which minimized the effect of age within the revised Geneva score.

The use of Wells score has been under debate for the presence of a subjective criterion, the physicians' judgment of whether "an alternative diagnosis is less likely than PE". It has been shown that the physician's decision to assign the score for this criterion was influenced by the simultaneous presence of one or more other variables in the Wells score [20]. However, the value of the clinical judgment remains crucial in the management of patients with clinically suspected PE [21].

On the other hand, in the revised Geneva score, the absence of an item related to immobilization for reasons other than surgery or fracture may tend to reduce the discriminant power of this clinical rule, particularly in elderly patients.

The role of the serum D-dimer is important, but limited to rule out PE in those cases with low or intermediate probability [22-24], because D-Dimer is characterized by low positive predictive value and specificity, as well as by high negative predictive value and sensitivity in the work-up of PE [22,25]. According to the Literature, D-dimer values greater than 500 ng/mL are considered positive [26], but there are many factors that can contribute to the elevation of a D-dimer value: advanced age, pregnancy, trauma, post-operative periods, inflammatory states and cancer [25]. Thus, in elderly people and in patients with renal dysfunction, the average D-dimer value tends to be higher, as recently emphasized by Righini et al. [27]. An age-adjusted D-dimer cut-off point (patient's age  $\times$  10 ng/mL), combined with clinical probability, can therefore increase the proportion of patients

older than 50 years, in whom PE could be safely excluded [28,29], so reducing the unnecessary exposure of these patients to radiation.

In conclusion, the better performance of Wells score and the use of serum D-Dimer in the assessment of clinical pre-test probability of PE in elderly patients hospitalized in a Department of Internal Medicine may suggest to carefully score patients older than 65 years even in absence of symptoms, in order to increase the diagnostic accuracy of this life-threatening disease state. The need for improving the diagnostic accuracy of Venous Thromboembolism (VTE) behind the Emergency Department is mandatory, given the increasing number of elderly patients with several comorbidities, who have access to the hospital and may develop VTE during hospitalization [13,30].

## References

- Horlander KT, Mannino DM, Leeper KV. Pulmonary embolism mortality in the United States, 1979-1998: an analysis using multiple-cause mortality data. *Arch Intern Med.* 2003; 163: 1711-1717.
- Goldhaber SZ, Visani L, De Rosa M. Acute pulmonary embolism: clinical outcomes in the International Cooperative Pulmonary Embolism Registry (ICOPER). *Lancet.* 1999; 353: 1386-1389.
- Nijkeuter M, Söhne M, Tick LW et al. The natural course of hemodynamically stable pulmonary embolism: Clinical outcome and risk factors in a large prospective cohort study. *Chest.* 2007; 131: 517-523.
- Stein PD, Matta F, Musani MH et al. Silent pulmonary embolism in patients with deep venous thrombosis: a systematic review. *Am J Med.* 2010; 123: 426-431.
- Le Gal G, Testuz A, Righini M et al. Reproduction of chest pain by palpation: diagnostic accuracy in suspected pulmonary embolism. *BMJ.* 2005; 330: 452-453.
- Guidelines on diagnosis and management of acute pulmonary embolism. Task Force on Pulmonary Embolism, European Society of Cardiology. *Eur Heart J.* 2000; 21: 1301-1336.
- Wells PS, Anderson DR, Rodger M et al. Derivation of a simple clinical model to categorize patients probability of pulmonary embolism: increasing the models utility with the SimpliRED D-dimer. *Thromb Haemost.* 2000; 83: 416-420.
- Moore LK, King CS, Holley AB. Current approach to the diagnosis of acute nonmassive pulmonary embolism. *Chest.* 2011; 140: 509-518.
- Le Gal G, Righini M, Roy PM et al. Prediction of pulmonary embolism in the emergency department: the revised Geneva score. *Ann Intern Med.* 2006; 144: 165-171.
- Ceriani E, Combescore C, Le Gal G et al. Clinical prediction rules for pulmonary embolism: a systematic review and meta-analysis. *J Thromb Haemost.* 2010; 8: 957-970.
- Penaloza A, Melot C, Motte S. Comparison of the Wells score with the simplified revised Geneva score for assessing pretest probability of pulmonary embolism. *Thromb Res.* 2011; 127: 81-84.
- Wong DD, Ramaseshan G, Mendelson RM. Comparison of the Wells and revised Geneva score for the diagnosis of pulmonary embolism: an Australian experience. *Intern Med J.* 2011; 41: 258-263.
- Di Marca S, Cilia C, Campagna A, et al. Comparison of Wells and Revised Geneva Rule to Assess Pretest Probability of Pulmonary Embolism in High-Risk Hospitalized Elderly Adults. *J Am Geriatr Soc.* 2015; 63: 1091-1097.
- Klok FA, Kruisman E, Spaan J et al. Comparison of the revised Geneva score with the Wells rule for assessing clinical probability of pulmonary embolism. *J Thromb Haemost.* 2008; 6: 40-44.
- Chagnon I, Bounameaux H, Aujesky D et al. Comparison of two clinical prediction rules and implicit assessment among patients with suspected pulmonary embolism. *Am J Med.* 2002; 113: 269-275.
- Ye YP, Li YY, Chen J et al. The diagnostic values of Wells score and modified Geneva score for pretesting acute pulmonary embolism: a prospective study. *Zhonghua Nei Ke Za Zhi.* 2012; 51: 626-629.
- Guo XJ, Liu M, Guo YM, et al. A comparison of the predictive values of three clinical scoring systems for suspected acute pulmonary embolism based on multidetector CT angiography. *Zhonghua Jie He He Hu Xi Za Zhi.* 2009; 32: 119-123.
- Calisir C, Yavas US, Ozkan IR et al. Performance of the Wells and Revised Geneva scores for predicting pulmonary embolism. *Eur J Emerg Med.* 2009; 16: 49-52.
- Miniati M, Bottai M, Monti S. Comparison of 3 Clinical Models for predicting the probability of Pulmonary Embolism. *Medicine.* 2005; 84: 107-114.
- Klok FA, Zidane M, Djurabi RK et al. The physician's estimation 'alternative diagnosis is less likely than pulmonary embolism' in the Wells rule is dependent on the presence of other required items. *J Thromb Haemost.* 2008; 99: 244-245.
- Moore LK, Collen JF, Woods KM et al. Practical utility of clinical prediction rules for suspected acute pulmonary embolism in a large academic institution. *Thromb Res.* 2004; 113: 1-6.
- Chopra N, Doddamreddy P, Grewal H et al. An elevated D-dimer value: a burden on our patients and hospitals. *Int J Gen Med.* 2012; 5: 87-92.
- Guidelines on diagnosis and management of acute pulmonary embolism. Task Force on Pulmonary Embolism, European Society of Cardiology. *Eur Heart J.* 2008; 29: 2276-2315.
- Agnelli G, Becattini C. Acute pulmonary embolism. *N Engl J Med.* 2010; 363: 266-274.
- Fedullo PF, Tapson VF. Clinical Practice. The evaluation of suspected pulmonary embolism. *N Engl J Med.* 2003; 349: 1247-1256.
- Ouellette DR. Pulmonary embolism. 2008.
- Righini M, Van Es J, Den Exter PL, et al. Age-adjusted D-dimer cutoff levels to rule out pulmonary embolism: the ADJUST-PE study. *JAMA.* 2014; 311: 1117-1124.
- Harper PL, Theakston E, Ahmed J, et al. D-dimer concentration increases with age reducing the clinical value of the D-dimer assay in the elderly. *Intern Med J.* 2007; 37: 607-613.
- Douma RA, Le Gal G, Sohne M, et al. Potential of an age-adjusted D-dimer cut-off value to improve the exclusion of pulmonary embolism in older patients: a retrospective analysis of three large cohorts. *Br Med J.* 2010; 340: c1475.
- Malatino L, Cardella AM, Puccia G, Cilia C, Terranova V, Cataudella E, et al. Testing Clinical Scores to Diagnose Incident Deep Vein Thrombosis in Patients Hospitalized in a Department of Medicine: Can Biomarkers Improve Accuracy? *Angiology.* 2016; 67: 245-251.