International Journal of Healthcare Sciences ISSN 2348-5728 (Online)
Vol. 4, Issue 2, pp: (854-860), Month: October 2016 - March 2017, Available at: www.researchpublish.com

Pulmonary Embolism in Family Practice Care; Systematic Review

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Abstract: **Pulmonary embolism (PE) is a relatively common acute cardiovascular disorder with high early mortality rates. the incidence of PE is estimated to be approximately 60 to 70 per 100,000, and that of venous thrombosis approximately 124 per 100,000 of the general population. This Systematic review study aimed to overview the pulmonary embolisms from different perspectives in family practice (primary care), we intended to discuss the role of early diagnosis and approaches to do so, also to evaluate the management available options in primary care for pulmonary embolisms. We conducted a systematic review study, through search in literature among Medline and the Database of Abstracts and Reviews (DARE) to identify identified clinical studies and systematic reviews. We searched Medline for English language publications and the Cochrane Database of Systematic Reviews up to December 2016. Several studies compared the predictive worth of the gestalt and medical choice rule when utilized in combination with D-dimer testing for leaving out lung embolism. The level of sensitivity of gestalt was similar to medical rules (Wells, Geneva, Revised Geneva) however its uniqueness was lower. Using a point of care D-dimer test integrated with the Wells rule worked in reducing false positives. other evidence stated that the Family Physicians appear with apparently gave concern to sensitivity rather than uniqueness in role of diagnosis of PE.**

Keywords: **Pulmonary embolism (PE), Database of Abstracts and Reviews (DARE).**

1. INTRODUCTION

Pulmonary embolism (PE) is a relatively common acute cardiovascular disorder with high early mortality rates [(1)]. the incidence of PE is estimated to be approximately 60 to 70 per 100,000, and that of venous thrombosis approximately 124 per 100,000 of the general population [(2,3)]. The European guidelines for the diagnosis and management of PE report annual incidence rates of venous thrombosis and PE of approximately 0.5 to 1.0 per 1000 inhabitants [(4)]. However, the actual figures are likely to be substantially higher because silent PE can develop in up to 40% to 50% of patients with deep vein thrombosis (DVT) [(5)]. In addition, autopsy studies have shown that PE had been diagnosed before death in 30% to 45% of patients [(6)]. After coronary artery disease and stroke, acute PE ranks third among the most common types of cardiovascular diseases. While clinical data indicate that most cases of PE occur at 60 to 70 years of age, autopsy data show the highest incidence among individuals 70 to 80 years of age. If untreated, acute PE is associated with a significant mortality rate (as high as 30%), whereas the death rate of diagnosed and treated PE is 8%. Up to 10% of acute PE patients die suddenly [(6,7)].

PE is readily diagnosed in patients presenting with DVT. The most common sources of PE (up to 85% of cases) include DVT followed by thrombosis of iliac and renal veins, and the inferior vena cava. The upper limbs are not usually identified as a source of major PE [(7)]. Venous thromboembolism (VTE) is believed to result from an interaction of the individual patient's risk factors and the setting or circumstances where it occurs. Patient-associated risk factors are usually permanent, whereas the circumstances tend to be transient in nature. Patient risk factors include age, personal history of VTE, active malignancy or another disabling conditions such as heart or respiratory failure, congenital or acquired

coagulation disorders, hormone replacement therapy and oral contraception. According to the British Thoracic Society, risk factors are traditionally classified into major and minor categories (**TABLE 1**) [8].

Family physician at primary care are a very serious situation deciding whether or not to send a low-risk patient to healthcare facility for further screening one must stabilize the harm as outcome of missing the diagnosis versus the damage associated with the diagnostic assessment and the harm induced by treatment. Kline determined a test limit of 1.8% [9,10]. Patients with a pretest likelihood listed below this limit ought to not go through further testing for PE. Another approach was used in the Christopher research study with a point quote limit of 1.7% being the ceiling of the series of identified VTE in a three-month follow-up duration after an unfavorable lung angiography [11]. In a current research study, we showed that utilizing the Wells decision guideline and a (more sensitive but less specific) quantitative D-Dimer test instead of a (less sensitive but more particular) qualitative D-dimer test, is more safe (only one failure) however with more patients unnecessarily exposed to CT-scanning [12]. When omitting PE one needs to stabilize between a strategy with less failures however more patients unnecessarily exposed to CT-scanning, versus a less safe strategy with fewer patients exposed to CT-scanning [12].

TABLE 1: Risk factors of venous thromboembolism, according to the British Thoracic Society, 2003 [8]

Major risk factors (RR = 5 to 20)	Minor risk factors (RR = 2 to 4)
1. **Postoperative states:** Major abdominal/pelvic surgery, hip/knee joint replacement, postoperative intensive care 2. **Obstetrics**: Late pregnancy, Caesarian section, puerperium 3. **Lower limb affections:** Fractures, extensive varicosities 4. **Malignancies:** Abdominal/pelvic, advanced/metastatic stage 5. **Limited mobility:** Hospitalization, geriatric care 6. **Miscellaneous:** History of previous venous thromboembolism	I. **Cardiovascular:** Congenital heart disease, heart failure, hypertension, superficial venous thrombosis, central venous catheter I. **Humoral:** Estrogen use: oral contraception, hormone replacement therapy I. **Miscellaneous:** Chronic obstructive lung disease, neurological impairment, latent malignancy, thrombotic defects, long-distance travel in the sitting position, obesity . **Other:** Inflammatory bowel disease, nephrotic syndrome, chronic dialysis, myeloproliferative disease, paroxysmal nocturnal hemoglobinuria

Objectives:

This Systematic review study aimed to overview the pulmonary embolisms from different perspectives in family practice (primary care), we intended to discuss the role of early diagnosis and approaches to do so, also to evaluate the management available options in primary care for pulmonary embolisms

2. METHODOLOGY

Search Method:

We conducted a systematic review study, through search in literature among Medline and the Database of Abstracts and Reviews (DARE) to identify identified clinical studies and systematic reviews. We searched Medline for English language publications and the Cochrane Database of Systematic Reviews up to December 2016, using the following combination of medical subject headings, text words, and publication types:

("pulmonary embolism" or "PE") and ("D dimer" or "DVT" or "Family practice, general practice" or "primary care" Deep venous thrombosis, and diagnosis or Management of PE in primary care).

We also searched reference lists of identified articles to ensure identification of all relevant articles. Search terms including all studies that matches our search criteria of such meta-analyses; clinical trials; and randomized, controlled trials. Two authors independently reviewed the titles and abstracts of the references identified to determine suitability for inclusion and they extracted the data. If disagreement arose all three authors conferred to reach consensus.

3. RESULTS & DISCUSSION

➢ **Pathophysiological considerations:**

The severity of acute PE is determined primarily by its hemodynamic impact, presenting as unexpected lung hypertension. A critical function in the supreme hemodynamic effect is likewise played by cardiovascular practical status ('cardiovascular reserve'), as well as adjustment of neurohumoral and pulmonary systems. In fact, even a morphologically substantial PE can provide as a hemodynamically small one and vice versa (**Figure 1**) [(1)]. It is traditionally believed that patients without a history of heart or pulmonary disease need pulmonary bed blockage of 30% to 50% to establish lung hypertension [(13)]. In patients with a heart or lung disease, nevertheless, even a minor blockage in the lung flow is sufficient to cause pulmonary hypertension. The contribution of humoral and reflex pulmonary vasoconstriction reported in an experimental setting is not considered to be relevant in clinical practice. The acutely establishing lung hypertension in PE leads to a boost in RV afterload, morphologically presenting as RV dilation and might ultimately trigger right-heart failure. As soon as pulmonary vascular resistance has actually risen to a level that the Recreational Vehicle is unable to endure, PE can lead to sudden death through pulseless electrical activity (formerly electromechanical dissociation) or asystole (**Figure 2**) [(1)].

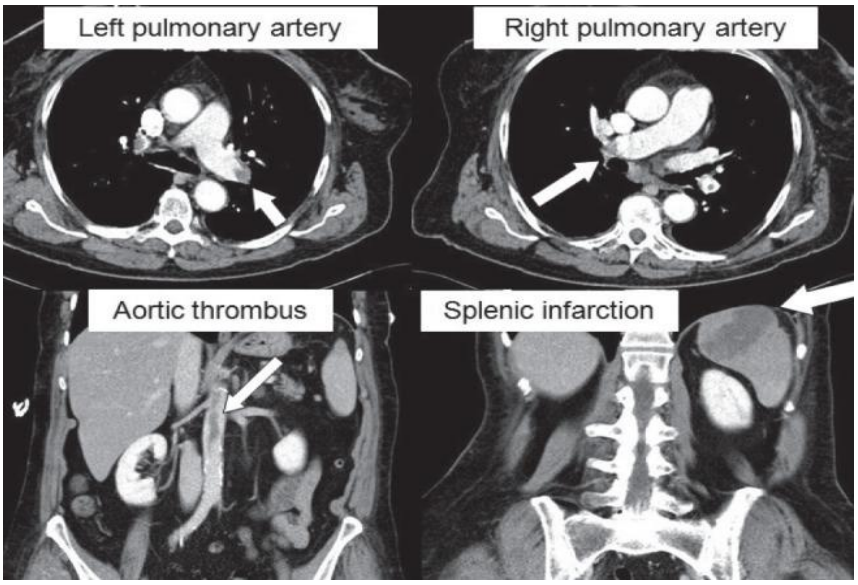

Figure1: A female patient with clinically small (ie, hemodynamically not significant), yet morphologically extensive, pulmonary embolism (arrows point to large emboli in the left and right pulmonary artery branches on computed tomography angiography). [(1)]

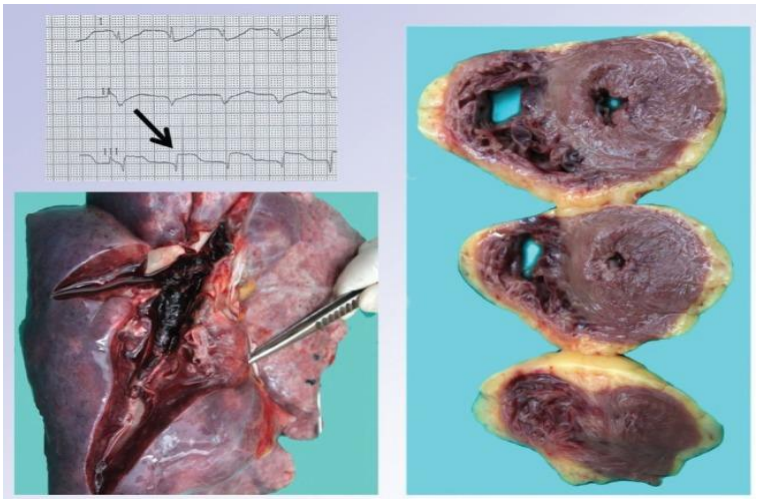

Figure2: Massive pulmonary embolism in a 35-year-old woman presenting with cardiac arrest and asystole. The patient was brought in by emergency medical services under continuous resuscitation; transient resumption of electrical activity was followed by clear ST-segment elevations in lead III (upper left panel). [(1)]

- **Clinical presentation very important for family physicians take an immediate action:**

Prompt recognition of a PE is crucial because of the high associated mortality and morbidity, which may be prevented with early treatment. Failure to diagnose PE is a serious management error since 30% of untreated patients die, while only 8% succumb with effective therapy [14]. Unfortunately, PE may be asymptomatic or present with sudden death. Characteristic signs and symptoms such as tachycardia, dyspnea, chest shock, hypoxemia, and pain are non-specific and are present in many other conditions, such as acute MI, congestive heart failure, or pneumonia. In the Prospective Investigation of Pulmonary Embolism Diagnosis II (PIOPED II) trial, patients with PE had a range of signs and symptoms. Common signs were tachypnea (54%) and tachycardia (24%). The most common symptoms were dyspnea, usually of onset within seconds, at rest or with exertion (73%), pleuritic pain (44%), calf or thigh pain (44%), calf or thigh swelling (41%), and cough (34%) [15].

- **Clinical Decision Rule and D-Dimer Assay in Patients with clinically suspected pulmonary in Primary care:**

D-dimer (DD) screening and imaging, such as helical multidetector computed tomography (MDCT). Proof from recent research studies suggests that the occurrence of PE among patients who undergo diagnostic work-up has actually decreased from 30% to below 10% (16), perhaps as a consequence of the wide availability of DD testing that may reduce physicians' threshold of scientific suspicion and result in overtesting. While a negative, extremely delicate DD test reliably excludes venous thromboembolism (VTE) in patients with a non-high medical pretest possibility, DD tests have a low uniqueness, resulting in false-positive result rates of 50% or more [17]. Due to the fact that positive D-dimer outcomes are usually followed by pricey additional tests (normally MDCT), the high false-positive test rate exposes many patients to unneeded risks, such as contrast-induced allergic reactions and nephropathy, or the postponed occurrence of radiation-induced solid tumors [18,19,20]. Because of the variable nature of the discussion of PE, the assessment largely depends on the probability of PE and the stability of the patient. There are scoring systems to help in the determination of possibility of PE and thromboembolic events. Diagnostic scoring systems such as the Wells requirements and Geneva rating are often utilized. The Pulmonary Embolism Rule-out Criteria (PERC) guideline was developed to recognize patients at such a low pre-test risk for PE that PE can securely be excluded without the requirement for DD screening, thus preventing false-positive DD results [21] and the dangers of unnecessary testing. The guideline is based on 8 medical requirements **(Table 2 A&B)** [22,23]. Patients who fulfill these eight criteria are determined as PERC-negative [PERC $_{(-)}$] and appear to have an extremely low pretest probability of PE, with a residual risk of PE much like the risk after a typical pulmonary angiogram [24].

Table 2. The Pulmonary Embolism Rule-out Criteria (PERC) rule (A) and the revised Geneva score (B) [22,23]

(A) The Pulmonary Embolism Rule-out Criteria (PERC) rule [22] *	
Age < 50 years	
Pulse < 100 bpm	
Pulse oxymetry > 94%	
No unilateral leg swelling	
No hemoptysis	
No surgery or trauma within 4 weeks	
No prior deep vein thrombosis or pulmonary embolism	
No oral hormone use	
*Patients who meet all of these eight criteria are considered to be at a very low risk for pulmonary embolism.	
(B) The revised Geneva score [23]	
Risk factors	**Points**
Age > 65 years	1
Previous deep vein thrombosis or pulmonary embolism	3
Surgery (under general anesthesia) or fracture (of the lower limbs) within 1 month	2
Active malignant condition (solid or hematologic malignant condition, currently active or considered cured < 1 year)	2
Unilateral lower limb pain	3
Hemoptysis	2
Heart rate	
75–94 beats min−1	3
≥ 95 beats min−1	5
Pain on lower-limb deep venous palpation and unilateral edema	4
Clinical probability	
Low	0–3
Intermediate	4–10
High	≥ 11

A series of retrospective and potential recognition research studies showed that $PERC_{(-)}$ patients have a risk of PE varying between 0% and 1.4% [22,24,25,26]. Nevertheless, these recognition research studies included selected patients who were at low risk for PE (e.g. patients with a low possibility of PE based upon physician assessment or with pleuritic chest pain just) or were restricted by a small sample size [22,24,25,26]. The frequency of PE only differed in between 5.3% and 12% in these studies [22,24,25,26,27]. When applied to a sample of unselected patients with an overall PE occurrence of 26%, 6.7% of $PERC_{(-)}$ patients had PE, a percentage that is unacceptably high [28]. It has actually therefore been suggested that the PERC guideline should be used only to patients at a really low risk for PE, which requires the application of another PE medical choice guideline [29].

If a patient satisfies all of the PERC criteria and has a low possibility of PE by Wells criteria and the gestalt opinion of the examining physician, then a PE might be ruled out [22]. In reality, very few patients satisfy these criteria and the PERC assessment is not reliable for the in-hospital setting. The previously mentioned tools: Wells rating, Geneva score, and PERC work best in examining the requirement for further work-up of stable patients providing to the emergency room; with inpatients and critically ill patients, such tools are not as trustworthy. The aspects of diagnostic workup will differ depending on whether the patient is hospitalized and whether there is hemodynamic instability. In a patient with a believed PE, medical diagnosis of proximal DVT in a symptomatic patient, or in an asymptomatic patient who has contraindications to CT angiography, suffices to rule in PE [30]. In a steady patient, providing from an outpatient setting, who has not sustained recent injury or surgery, a d-dimer test should be performed. If negative, and clinical suspicion is low, then the possibility of PE is additional and low workup is unnecessary. d-Dimer is a deterioration item of cross-linked fibrin that is formed immediately after fibrin clots are degraded by plasmin and reflects an international activation of blood coagulation and fibrinolysis. Therefore, d-dimer is not a helpful test in post-operative patients since it will rise due to coagulation and fibrinolysis [30].

- **Assessing clinical suspected PE in primary care:**

There are several scoring systems and designs of medical likelihood of PE, which are consisted of in both presently offered guidelines for the medical diagnosis and management of PE [3,4] (eg, one developed by Wells, or the revised Geneva rating). The scores are not commonly used in scientific practice. The most recent meta-analysis failed to show their adequacy in last exclusion of PE [31]. As pointed out above, what in fact matters is the possibility of PE; after this, it is typically straightforward to rule or confirm out the diagnosis utilizing other laboratory tests. Nevertheless, stand-alone lab investigations and clinical imaging, especially with D-dimers or CTA, might not have clinical significance, and may be detrimental and/or financially inefficient to the patient [32,33,34].

In 2011, Lucassen et al [31] assessed the efficiency of gestalt and forecast designs for detecting PE in a meta-analysis. They discovered significant heterogeneity among the research studies evaluating gestalt; for instance, the thresholds for low probability used varied from 10% to 40% throughout studies. All studies were performed in a secondary care setting. Our existing findings, nevertheless, remain in line with the primary conclusions of that meta-analysis: family physicians do extremely well in securely excluding patients at extremely low risk by combining gestalt with d-dimer screening, yet at the cost of referring (many) more patients as compared with using a formal decision rule. Barais et al [35] carried out a qualitative research study in a French medical care setting. Utilizing semistructured interviews, they intended to specify the procedure preceding a validated diagnosis of PE. For all interviewed family doctor, the diagnostic procedure was mainly owned by user-friendly factors, highlighting the value of contextual understanding and proof in primary care. Provided the qualitative nature of this study, nevertheless, it does not supply information on whether gestalt or a prediction design is better for efficiently and safely recognizing low-risk patients [35].

4. CONCLUSION

Several studies compared the predictive worth of the gestalt and medical choice rule when utilized in combination with D-dimer testing for leaving out lung embolism. The level of sensitivity of gestalt was similar to medical rules (Wells, Geneva, Revised Geneva) however its uniqueness was lower. Using a point of care D-dimer test integrated with the Wells rule worked in reducing false positives. The Family Physicians appear with apparently gave concern to sensitivity rather than uniqueness. The absence of indicative clinical signs for diagnoses other than PE, a sudden change in the condition of the patient, and the Family Physicians experience of formerly failing to identify PE, in addition to a sense of alarm were the main factors of the choice to refer. A choice guideline was not used at all. The sense of alarm was utilized as a tool to prevent the diagnostic mistake of missing a PE. The diagnostic accuracy of this aspect of gut feelings has to be assessed prior to being suggested or taught.

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