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Chapter 1

General introduction and outline
Pulmonary embolism (PE) refers to a blood clot in the pulmonary artery or one of its branches, which is most commonly originating from deep venous thrombosis (DVT) of the legs or pelvis. Venous thrombo-embolism (VTE) encompasses both pulmonary embolism (PE) and deep venous thrombosis (DVT) (1). VTE is the third most frequent cardiovascular disease and it is a major cause of mortality, morbidity and chronic disease and disability. In Europe, it affects 430,000 patients each year and worldwide the overall annual incidence is 100-200 per 100,000 inhabitants (2, 3).

The diagnostic process of patients with suspected PE is challenging due to the non-specific symptoms and clinical presentation. Integrated diagnostic algorithms including validated clinical decision rules, high sensitive D-dimer tests and imaging tests such as computed tomography pulmonary angiography (CTPA) may guide the clinician, and close adherence to the diagnostic algorithm is of crucial importance for the clinical outcome of patients with suspected PE (1, 2). The focus of this thesis is the diagnostic management of patients with suspected PE.

The first part of this thesis focuses on the diagnostic management of pregnant patients with suspected PE. During pregnancy, women have a 4 to 5 fold increased risk for venous thrombo-embolism (VTE) compared age matched non-pregnant women, and PE contributes to an important degree to maternal mortality in Western Europe; an accurate diagnosis of PE during pregnancy is thus of crucial importance (4-6). There are different reasons why the diagnosis of PE is challenging during pregnancy. First, many of the common VTE-symptoms are also associated with normal pregnancy, such as oedema, tachycardia and dyspnea, which makes PE more difficult to diagnose. Moreover, clinical decision rules and D-dimer tests have not been validated in the pregnant population (7, 8). An overview of the current diagnostic strategies of suspected PE -and the limitations thereof - in the pregnant population is presented in chapter 2. Imaging is the gold standard to confirm or rule out PE in the pregnant population, although associated with radiation exposure to mother and foetus. Both ventilation-perfusion scan and CTPA may be used for this purpose. In chapter 3, a meta-analysis is provided to compare the risks and results of these imaging tests in the pregnant population. A new safe and simplified diagnostic algorithm for patients with suspected PE, the YEARS algorithm, was evaluated in pregnant patients. Results of this prospective multinational, multicenter diagnostic management study are described in chapter 4.

The second part of this thesis focuses on the diagnostic management of unselected patients with suspected PE. The results of a sex-specific prevalence and performance of three different diagnostic algorithms from seven prospective management studies are described in chapter 5. The aim of this study was to evaluate the efficiency and failure rate of three different diagnostic strategies in men versus women and to determine the sex-specific prevalence of PE.
Different strategies to reduce the number of required CTPA’s and to improve the efficiency for excluding PE have been published in the last decade, i.e. YEARS, ADJUST and PERC. The first strategy is the YEARS diagnostic algorithm, which consists of simultaneous assessment of three clinical YEARS-items and a D-dimer test in all patients (9). Using the YEARS algorithm resulted in an improved efficiency with a reduction of 14% in the need to perform CTPA with a very low three month VTE failure rate. Another strategy is the age-adjusted D-dimer cut-off in patients of 50 years and older, defined as patients’ age x 10 ng/ml as threshold (ADJUST) (10, 11). In chapter 6 the combination of this age-adjusted D-dimer threshold with the YEARS algorithm was evaluated to investigate if this combination could potentially further improve the efficiency in the diagnostic work-up of patients with suspected PE. A third strategy to improve the efficiency of the diagnostic management of patients with suspected PE is the use of the pulmonary embolism rule-out criteria (PERC) (12, 13). This rule involves eight clinical items, and when all the items are scored negative, PE is ruled out without further diagnostic tests. Chapter 7 evaluates the combination of this PERC rule and the YEARS algorithm.

Since the YEARS algorithm is easier to apply in daily clinical practise in comparison with the conventional algorithm, it may provide additional benefits over more improved efficacy, i.e. less CT scans with comparable safety. Chapter 8 provides an overview of the total time of an emergency department visit for patients with suspected PE and the associated costs when using the YEARS algorithm in comparison with the conventional algorithm. The aim of chapter 9 was to evaluate if chest X-ray results differ between patients with confirmed PE and with PE ruled out and to investigate whether chest X-ray provides incremental diagnostic value to the YEARS criteria when selecting patients with an indication for CT-scan. Lastly, since the introduction of multi-detector CT-scan, the sensitivity for visualizing smaller PE has noticeably advanced (14). These advances have led to a more frequent detection of filling defect in the smaller pulmonary arteries or subsegmental arteries. The prevalence of these small emboli – subsegmental PE – in patients with suspected PE using the YEARS algorithm was compared to the conventional algorithm in chapter 10.
REFERENCES