Effect of age on the assessment of clinical probability of pulmonary embolism by prediction rules

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Effect of age on the assessment of clinical probability of pulmonary embolism by prediction rules

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The incidence of venous thromboembolism increases with age [1]. Among individuals aged 60–74 years, the annual incidence of venous thromboembolism is about 3.5 per 1000. These rates are increased about 3-fold (nine per 1000) among individuals aged more than 75 years [2]. Pulmonary embolism (PE) is also associated with a greater short-term mortality among elderly people compared with younger patients [3]. PE can mimic a vast number of cardiopulmonary diseases, particularly in elderly patients in whom it remains a diagnostic challenge. Contemporary diagnosis of PE rests on sequential diagnostic strategies usually including clinical probability, D-dimer test, compression ultrasonography (US) of the lower limbs, ventilation-perfusion lung scan or helical computed tomography (CT) and angiography [4–6].

Age influences the performance of diagnostic tests currently used for PE. The diagnostic yield of D-dimer and ventilation-perfusion lung scan is reduced in elderly patients [7], while that of lower limb venous compression US increases in parallel with the increasing proportion of patients with PE-associated deep vein thrombosis with older age [8]. On the other hand, the performance of single-detector helical CT is not influenced by increasing age [9], and similar results may be expected for multidetector helical CT.

Assessment of clinical probability is an important step in the diagnostic approach to PE, as it allows identification of patients at lower risk of the disease who require a less extensive diagnostic work-up. For instance, the association of a low clinical probability of PE and low D-dimer concentration has been shown to safely rule out PE [4]. Assessment of clinical probability may be empiric or based upon prediction rules or scores. Two scores have been described and validated: the Wells' score [10] and the Geneva score [11]. In a recent study, the Wells' score and the Geneva score with possible implicit override demonstrated similar performances. These rules were derived and validated in patient populations with a wide age range. We hypothesized that older age may decrease the diagnostic performance of both scores as clinical presentation may be less typical and differential diagnosis be wider in elderly patients.

Therefore, we analyzed a database of 965 consecutive outpatients with suspected PE that were included in a prospective management study whose main objective was the validation of a diagnostic strategy based upon clinical probability assessment, D-dimer measurement, venous US and helical CT. A low or intermediate clinical probability allowed the ruling out of the diagnosis of PE if D-dimer levels were $< 500\ \mu g\ L^{-1}$ or if both proximal US and helical CT were negative. In patients with a high clinical probability, a pulmonary angiogram was required even if all other tests were negative. All patients were followed up during 3 months. The overall prevalence of PE was 23%. The studied diagnostic strategy was safe and effective, as assessed by a 3-month thromboembolic risk that was about 1% [12]. To evaluate the effect of age on the performance of these two prediction rules, we arbitrarily divided our population into three age categories: < 50 years, 50–74 years, and ≥ 75 years. Clinical probability was assessed by a prediction rule, the Geneva score, combined

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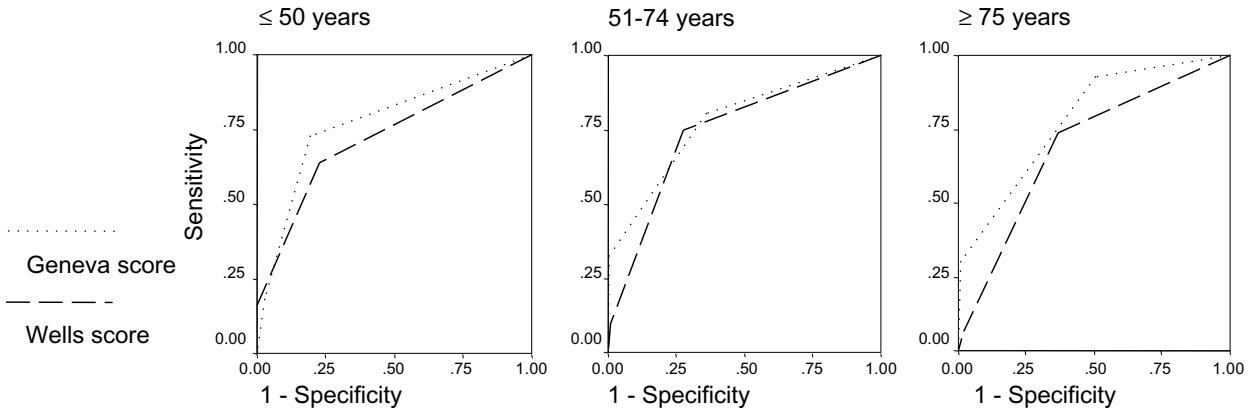

	Low	Interm.	High	Low	Interm.	High	Low	Interm.	High
Geneva overridden score									
Prevalence of PE	5.4	35.8	53.3	8.6	29.6	96.4	6.0	34.7	92.3
Number of patients	*221*	*67*	*15*	*186*	*135*	*28*	*100*	*144*	*26*
AUC* (SD)	0.78 (0.69-0.86)			0.78 (0.72-0.84)			0.78 (0.72-0.84)		
Wells' score									
Prevalence of PE	7.4	26.3	100	9.8	43.2	80.0	14.9	45.0	55.6
Number of patients	*216*	*80*	*7*	*214*	*125*	*10*	*141*	*120*	*9*
AUC* (SD)	0.72 (0.63-0.81)			0.75 (0.68-0.81)			0.69 (0.62-0.76)		

* AUC : Area Under Curve

Fig. 1. Performance of prediction rules among three age groups displayed as ROC curves.

with implicit judgement (in case of disagreement with the prediction rule, physicians in charge of the patient could override the rule by implicit probability assessment in both directions) [13]. The Wells' score was computed secondarily from the database, except in 43 patients, due to missing data, leaving a sample of 922 patients for whom both scores were available. Prevalence of PE in the three age categories was 44/330 (15%), 83/349 (24%) and 80/270 (30%), respectively.

We calculated the sensitivity and the specificity values for both prediction rules in each age category and displayed the data as receiver–operating characteristic (ROC) curves. Analysis of the area under the curve was used to evaluate the performances of these scores according to age. As shown in Fig. 1, the performances of both scores were quite similar. Moreover, even in the patients > 75 years, both prediction rules were able to identify reliably three categories of patients with increasing prevalence of the disease, which is the crucial issue to guide the diagnostic work-up.

We therefore conclude that assessment of clinical probability by both the Wells' score and the Geneva score with possible override by implicit evaluation is reliable, whatever the age category, and their use should be encouraged even in elderly patients.

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Potassium homeostasis in patients receiving prophylactic dose enoxaparin therapy

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Unfractionated heparin (UFH), the mainstay of anticoagulation therapy for more than 50 years, is associated with an increased risk of bleeding, heparin-induced thrombocytopenia, thrombosis, osteoporosis and alopecia [1]. Another known but often overlooked complication of UFH therapy is hyperkalemia [2–5]. It is not clearly known if low-molecular weight heparins (LMWH) have an inhibitory effect on aldosterone similar to UFH that translates clinically as hyperkalemia.

Potassium homeostasis is partly regulated by kidney and controlled by renin–angiotensin–aldosterone system. Urinary potassium excretion is a function of potassium concentration in the lumen of the cortical collecting duct (CCD) times the urine flow rate [6]. Determining the transtubular potassium concentration gradient (TTKG) is a novel clinical approach to estimate the urinary potassium excretion. It is considered an easy and sensitive method for the evaluation of mineralocorticoid action in the distal and collecting tubules [7,8]. We conducted a prospective study to determine the effect of enoxaparin (Lovenox®, Aventis Pharmaceuticals Inc, Bridgewater, NJ, USA) on the aldosterone-mediated renal handling of potassium balance.

An appropriate approval for our study was obtained from the institutional review boards of the participating institutions, the Veterans' Affairs Medical Center and Meritcare Medical Center, Fargo, North Dakota. Between 2001 and 2003, 78 patients (48 males and 30 females; mean age: 67 years) who underwent an elective total hip or knee arthroplasty were included. We excluded patients with clinical conditions that could interfere in potassium homeostasis and act as confounding variables to include: history of diabetes mellitus, renal failure, patients on angiotensin converting enzyme inhibitors/angiotensin receptor blocker therapy, and patients on potassium supplements, non-steroidal anti-inflammatory drugs, and diuretics. All patients were started on LMWH therapy using enoxaparin for prophylaxis (30 mg subcutaneously every 12 h for the duration of at least 4 days) against postoperative deep venous thrombosis and had adequate renal function (creatinine clearance ≥ 90 mL min^{-1}). Baseline serum potassium, creatinine and osmolarity, as well as baseline urinary sodium and potassium concentration and urinary osmolarity were monitored from all patients prior to the initiation of LMWH therapy and re-evaluated after 4 days of LMWH therapy. Transtubular potassium concentration gradient was calculated 1-day prior and again 4 days after LMWH therapy was initiated. If the urine osmolarity were lower than serum osmolarity, the calculation of TTKG would be unreliable [6]. Thus, only 67 of the 78 patients included in our study were eligible for TTKG calculations. Statistical analysis was done using SPSS-10® for Windows®. Wilcoxon signed rank test was used to analyze differences in the mean serum potassium levels and TTKG, before and after LMWH therapy.

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Effect of LMWH on serum potassium concentration

Serum potassium concentrations before and after LMWH therapy were obtained and analyzed in the 73 of 78 patients who entered the study. Mean (± SD) serum potassium concentration before LMWH was 4.05 (± 0.30) mmol/dL. It increased to 4.37 (± 0.41) mmol/dL after LMWH therapy. Although, the mean increase in serum potassium post-LMWH treatment in our study population was 0.3 mmol dL^{-1}, this was not statistically significant ($P = 0.07$).

Effect of LMWH on TTKG

Only 67 of 78 patients were candidates for a reliable TTKG calculation. The mean (± SD) calculated TTKG was 5.57 (± 2.4) before LMWH therapy and the mean (± SD) TTKG calculated 5 days after initiating LMWH was 5.90 (± 3.0). The mean change in TTKG (an increase of 0.33) was not statistically significant ($P = 0.54$).