



South African guidelines on venous thromboembolism

To the Editor: We commend the excellent work by Jacobson *et al.* on behalf of the South African Society of Thrombosis and Haemostasis in producing a very necessary set of local guidelines on the management of venous thromboembolism (VTE).¹ VTE is a major cause of morbidity and mortality, as highlighted recently by the United States Surgeon General.² One important nuance worth noting, however, is the fact that warfarin may be started together with low-molecular-weight heparin (LMWH) on day 1 of anticoagulation, and is supported by recent guidelines by the British Committee for Standards in Haematology and the American College of Chest Physicians (ACCP) who both agree that LMWH and warfarin should be started on the same day.^{3,4} The ACCP gives this recommendation their highest level of evidence, namely 1A. Evidence for this suggestion includes data from a randomised trial by Mohiuddin *et al.* showing decreased cost and morbidity in the group started earlier on warfarin.⁵ Leroyer *et al.* and Gallus *et al.* have both also shown decreased duration of hospitalisation with earlier initiation of warfarin.^{6,7} The ACCP also recommends that the duration of LMWH should be for a minimum of 5 days v. the 7 days suggested by Jacobson *et al.* This is in part based on at least one randomised trial showing similar efficacy in both arms.⁸ Although this may only result in a total difference of 4 doses of LMWH per patient, the long-term cost implications may be significant. Lastly, noting the narrow therapeutic window of warfarin, we believe that it is important to consider major risk factors for bleeding on anticoagulants, such as increased age, uncontrolled hypertension, alcohol, use of non-steroidal anti-inflammatory drugs, liver disease and peptic ulcer disease, before initiating therapy.^{9,10}

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1. Jacobson BF, Louw S, Mer M, *et al.* Venous thromboembolism – prophylactic and therapeutic practice guideline. *S Afr Med J* 2009; 99: 467-473.
2. Surgeon General's Calls To Action. Rockville, MD, USA: Office of the Surgeon General. <http://www.surgeongeneral.gov/library/calls/index.html> (accessed 7 July 2009).
3. Winter M, Keeling D, Sharpen F, Cohen H, Vallance P. Procedures for the outpatient management of patients with deep venous thrombosis. *Clin Lab Haematol* 2005; 27: 61-66.
4. Hirsh J, Guyatt G, Albers GW, Harrington R, Schunemann HJ. Antithrombotic and thrombolytic therapy, 8th ed. *Chest* 2008; 133: 71-109.
5. Mohiuddin SM, Hilleman DE, Destache CJ, Stoysich AM, Gannon JM, Sketch MH. Efficacy and safety of early vs late initiation of warfarin during therapy in acute thromboembolism. *Am Heart J* 1992; 123: 729-732.
6. Leroyer C, Bressollette L, Oger E, *et al.* Early versus delayed introduction of oral vitamin K antagonists in combination with low-molecular-weight Heparin in the treatment of deep vein thrombosis. *Haemostasis* 1998; 28: 70-77.
7. Gallus A, Jackaman J, Tillett J, Mills W, Wycherley A. Safety and efficacy of warfarin started early after submassive venous thrombosis or pulmonary embolism. *Lancet* 1986; 2: 1293-1296.
8. Hull RD, Raskob GE, Rosenbloom D, *et al.* Heparin for 5 days as compared with 10 days in the initial treatment of proximal venous thrombosis. *N Engl J Med* 1990; 322: 1260-1264.
9. Wells PS, Forgie MA, Simms M, *et al.* The outpatient bleeding risk index: validation of a tool for predicting bleeding rates in patients treated for deep venous thrombosis and pulmonary embolism. *Arch Intern Med* 2003; 163(8): 917-920.
10. Kuijper PM, Hutton BA, Prins MH, Büller HR. Prediction of the risk of bleeding during anticoagulant treatment for venous thromboembolism. *Arch Intern Med* 1999; 159(5): 457-460.

Professor Jacobson replies: On behalf of the authors, I thank Webb *et al.* for their valuable comments.

The initiation of anticoagulation with LMWH and delaying warfarin was done knowingly for the following reason: South Africa has a nursing crisis aggravated in the State sector where LMWH is often only dispensed as a Schedule 7 medication. This leads to delays in patients receiving their LMWH. In our experience, numerous patients are therefore given warfarin, and LMWH is only given by nursing staff 24 - 48 hours thereafter. As there is a serious theoretical concern that patients' thromboses – especially those with Protein S deficiencies – will be exacerbated, there was consensus that warfarin should only be started after the clinician was convinced that the LMWH had actually been injected rather than prescribed.

Regarding LMWH duration for a minimum of 5 days v. 7 days: this actually depends on when the patient is fully mobile, which we believe is far more important than looking at empirical days, especially as numerous patients are discharged early from hospital to recover at home.

Lastly, we fully agree that, when commencing any patient on anticoagulation, the risk/benefit needs to be assessed and individualised in relation to any contraindications for anticoagulation.