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Thigh-length compression stockings and deep vein thrombosis after stroke

Deep vein thrombosis (DVT) and pulmonary embolism (PE) are key complications after stroke that can lead to substantial morbidity and mortality. Rates of venous thromboembolism (VTE) were high in the past but have fallen,[1] reflecting increased use of early rehydration, mobilisation, and aspirin.[2,3] An additional intervention is the use of graduated compression stockings (GCS), the efficacy of which, although shown for surgery,[4] is unproven in stroke.[1,5]

In *The Lancet* today, Martin Dennis and colleagues[6] present the results of the CLOTS 1 trial, the first large assessment of the safety and efficacy of thigh-length GCS in patients with recent stroke. The CLOTS 1 trial is vitally important for stroke care. 2518 patients were recruited from 64 centres in Australia, Italy, and the UK (in the latter case, benefitting from the UK Stroke Research Network) within 3 days of admission after stroke, and were representative of patients entering stroke services. The primary outcome was symptomatic or asymptomatic DVT detected on compression Doppler ultrasound, or symptomatic DVT, in the popliteal or femoral veins occurring within 30 days of randomisation. The trial found that GCS did not reduce DVT, compared with no GCS (absolute reduction 0·5%, 95% CI -1·9% to 2·9%, number needed to treat 200). GCS did not affect key secondary outcomes, including components of the primary outcome, as well as PE, VTE, and death. Importantly, GCS did not seem to be beneficial in prespecified subgroups: patients treated early, those with leg weakness, and those not given concomitant anticoagulation. Equally importantly, the use of GCS was associated with a four-fold increase in skin ulcers and necrosis, and a non-significant increase in lower limb ischaemia. These results are supported by an earlier observational study that also found no benefit with GCS.[7]

These findings suggest that GCS do not work after stroke, although they do work after surgery.[4] This might reflect differences in patients' age, duration of immobility, and comorbidities. Alternatively, CLOTS 1 could have obtained the wrong result. First, the trial might have been too small since it was only powered to detect a 4% absolute reduction in the primary outcome. However, the logistics and health economics of administering GCS to

reduce DVT by, say, 2% are probably not worthwhile—for example, 24 stroke patients would need about 0·3 of a nurse per day just to measure and fit GCS, with an additional cost per patient of about £20 for the stockings (assuming three pairs per patient). Second, the rate of proximal DVT (the type most likely to lead to PE) was lower than planned (10% *vs* 12%), which will have reduced the power of the study. Third, the trial was necessarily unblinded; however, the detection of DVT was made blinded to therapy by removing GCS with sufficient time before ultrasound to allow skin indentations to disappear. Lack of treatment blinding could mean that investigators managed patients differently; the 0·8% excess use of anticoagulation in patients randomised to avoid GCS might indicate such a bias, although this is unlikely to have influenced the overall findings. Fourth, although centres were trained in the sizing and fitting of GCS, it is likely that both trial and clinical practice can result in the incorrect use of GCS; this practice would be ineffective or even hazardous. Last, compliance is important[7] and the CLOTS 1 Investigators report that this was only 79% in the first 14 days, and 73% up to 30 days.

What then should be used for VTE prophylaxis after stroke? CLOTS 2 is a comparison of thigh versus below-knee GCS, but this trial will now close early in view of the CLOTS 1 results. Intermittent pneumatic compression has also been studied[5,8] and CLOTS 3 is assessing this approach. Subcutaneous low-to-medium dose heparin is effective in reduction of VTE but unfortunately the reduction in PE, the primary target for prevention, is matched by a similar increase in symptomatic intracerebral haemorrhage and the absolute rates of both events are similar.[9–11] Worse still, the risk factors for VTE and symptomatic intracerebral haemorrhage are similar (eg, age and severity) so it is not possible to identify patients who are at high risk of VTE but not bleeding. Thus, prophylactic heparin cannot be recommended routinely after ischaemic stroke. However, low-molecular-weight heparin (which is more effective than unfractionated heparin[12] and only needs to be given once daily) should probably be used in patients who are at very high risk of VTE, such as those with previous VTE, known thrombophilia, or morbid obesity.

In summary, GCS do not reduce DVT or overall VTE in patients with recent stroke; indeed, they damage the skin and might promote limb ischaemia. GCS should not be used after stroke, and current guidelines[13,14] will need to be amended. No specific prophylaxis appears to be necessary, although early rehydration, mobilisation, and aspirin are key cornerstones of

good stroke care. Prophylactic heparin should be used only in patients at very high risk of VTE; routine use, as currently recommended in guidelines,[13,14] is not appropriate because of the increased risk of intracerebral haemorrhage. The role of GCS now needs to be assessed urgently in other settings where they might also lack efficacy, including in general medical patients.

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