Compression Hosiery to Avoid Post-Thrombotic Syndrome (CHAPS) Trial

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Worldwide approximately half of adults diagnosed with deep-vein thrombosis (DVT) of the lower limb will go on to develop the post-thrombotic syndrome (PTS). PTS is defined as chronic venous symptoms or signs secondary to DVT- including leg pain, oedema, venous ectasia and in 5% of patients progressing to venous ulceration[1]. Despite adequate anticoagulation, PTS remains a chronic health condition with significant financial burden for both patients and health services[2].

Treatment options for PTS are limited. In the first instance patients are usually offered graduated compression stockings (GCS); elasticated garments which exert the highest pressure at the ankle, reducing towards the knee. The pressure gradient supports vascular structures in the leg, preventing blood from pooling and improving tissue microcirculation and venous return[3]. However, studies evaluating their effectiveness in the prevention of PTS have been inconsistent due to high heterogeneity. A Cochrane review concluded that GCS initiated in the acute phase of DVT may prevent PTS but further evidence is needed to determine their benefit [4]. The European Society for Vascular Surgery (ESVS) Guidelines on the Management of Venous Thrombosis recommend early compression for patients with proximal DVT but note the need for further studies [5].

CHAPS (ISRCTN73041168) is an investigator led, multicentre, assessor blind, randomised controlled trial [6]. CHAPS aims to measure the difference in incidence of PTS at a median of 18 months follow up after first DVT (less than 3 weeks from diagnosis) between standard clinical care (anticoagulation)

and the intervention arm (a graduated compression stocking and the standard clinical care (anticoagulation)). The primary outcome is any incidence of PTS using the validated Villalta scale. The patient is diagnosed with PTS if they score 5 points or more on the scale, or if a venous ulcer is present. A score of 5-9 denotes mild disease, 10-14 moderate disease and 15 severe disease. The primary outcome will be recorded at fixed time points for all those randomised; at 6 and 12-months post-randomisation and at study end (estimated to be a median of 18 months, range 6 to 30-months). Secondary outcomes include incidence of venous ulceration (measured by the Villalta scale), change in employment status, change in disease-specific and generic quality of life as measured by the VEINES-QoL and EuroQoL (EQ5D) scales and adherence to stockings and anticoagulants as reported by the patient. A cost effectiveness analysis of GCS will be performed using an incremental cost-effectiveness ratio (ICER) from the EQ5D questionnaire, with appropriate sensitivity analysis. The target population are adults with symptomatic presentation of first proximal DVT (located in the popliteal, femoral, common femoral, iliac veins, or a combination), less than 3 weeks from diagnosis, who can provide full informed consent. Participants in both trial arms will receive anticoagulation for a minimum of 3 months. Compression in the intervention arm is specified by the protocol; European Class II (23- 32 mm Hg). The flow of participants through the trial can be seen in Figure 1.

A combination of self-reported adherence and stocking reordering behaviour will be used to adjudicate adherence to the intervention and anticoagulation. If one year adherence does not reach the requirements outlined in the protocol, the trial will terminate. A process evaluation of factors influencing adherence will be reported.

In a clinical setting, diagnosis of PTS is made on the development of specific clinical signs and symptoms in patients with a history of DVT. The CHAPS trial uses the Villalta Scale to assess the primary outcome. It is the most frequently used scale for PTS, has good inter-rater reliability and is easy to use.

CHAPS opened in February 2020, aiming to recruit 864 participants. The study will have 90% power at a 5% level of significance using a test of binomial proportions to detect an absolute reduction in the incidence of PTS of 10% (from 30% in the standard care arm to 20% in the stockings plus standard care arm), allowing for 10% loss to follow up. Soon after the study opened, recruitment was paused due to the COVID-19 pandemic. The coordinating centre made several amendments to allow it to re-open in 2021.

Conflicts of Interest

None to declare

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Figure 1. CHAPS Consort diagram