RCT on GCS/LMWH vs LMWH in VTE prophylaxis

GAPS: Graduated compression as an Adjunct to Pharmacoprophylaxis in Surgery

A Multi-Centre Randomised Clinical Trial

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on behalf of the GAPS Trial Investigators
Disclosure

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The views and opinions expressed herein do not necessarily reflect those of the HTA, NIHR, NHS or the Department of Health
The Clinical Problem

“In the UK pulmonary embolism following DVT in hospitalised patients would cause 25,000 preventable deaths each year if thromboprophylaxis is not given”
Limited evidence for how VTE prophylaxis is achieved

- Evidence base supporting UK NICE’s recommendations for the use of graduated compression stockings (GCS) for VTE prevention in the UK is rightly challenged as there is a dearth of RCTs to support practice

  Whittaker et al. BMJ 2013

- Lack of evidence for the additional benefit of GCS over and above the benefit of low molecular weight heparin (LMWH) alone in this context

  Zareba et al. BJS 2014
The additional benefit of graduated compression stockings to pharmacologic thromboprophylaxis in the prevention of venous thromboembolism in surgical inpatients

Rishi Mandavia, BSc, Joseph Shalhoub, PhD, Karen Head, MSc, and Alun H. Davies, DM, London, United Kingdom

- Single direct comparison between pharmacoprophylaxis and GCS + pharmacoprophylaxis. Hip surgery. No significant difference in VTE

- 22 RCT study arms
Pharmacological Thromboprophylaxis Alone
n=22 study arms

Point estimate of patients with VTE varied from 1.3% to 43.8%
Point estimate of patients with VTE varied from 0% to 16.3%

Significant heterogeneity precluded quantitative synthesis
Benefits vs Risks

• **If** GCS were to offer a reduction in VTE risk over and above LMWH, these benefits need to be weighed against the risks and disadvantages of GCS

  – Discomfort
  – Ischaemia
  – Blistering
  – Cost
  – Non-compliance
  – Need for staff assistance in wearing

  **Cost of purchasing and applying GCS to surgical patients in England estimated at £63.1 million per annum**
RCT Aim

To determine whether low dose LMWH alone is non-inferior to a combination of GCS and low dose LMWH for the prevention of VTE in adult elective surgical patients identified as being at moderate and high risk for VTE
Study Population

- Elective surgical patients
- Moderate or high risk of VTE according to the UK Department of Health VTE Risk Assessment
Outcome Measures

Primary Outcome: VTE within 90 days
Duplex ultrasound-proven new lower-limb DVT (symptomatic or asymptomatic)

+ Symptomatic PE (imaging confirmed)
up to 90 days post-randomisation

Secondary Outcomes
• Quality of life – EQ5D
• Compliance with stockings & LMWH
• Overall mortality

Safety Outcomes
• GCS-related complications
• Bleeding complications
• LMWH allergy
Study Design

- Seven-centre, UK-wide, open, randomised controlled trial
- Non-inferiority, group sequential trial design
Multi-Centre, Multi-Disciplinary

- Imperial (CI: Prof AH Davies, Co-Is: Dr C Baker, Mr J Shalhoub, Sr K Dhillon)
- Kings (PI: Prof BJ Hunt)
- Cambridge (PI: Mr M Gohel)
- Birmingham (PI: Prof AW Bradbury)
- Newcastle (PI: Prof G Stansby)
- Salisbury (PI: Dr T Everington)
- Southampton (PI: Prof D Warwick)

- CTU: CHaRT, Aberdeen (Co-I: Prof J Norrie)

- Thrombosis UK (Co-I: Ms A Stephens-Boal)
Exclusion Criteria

• Contraindications to LMWH / GCS
• Documented or known thrombophilia / thrombogenic disorder
• Requiring therapeutic anticoagulation
• Previous VTE
• Having intermittent pneumatic compression beyond theatre and recovery
• Pregnancy
• Need extended VTE prophylaxis
• Cast / brace use
Sample Size

- Assuming an event rate of 6% of VTE at 90 days in the combined group and non-inferiority margin of 3.5%
- Loss to follow up of 10%
- Maximum sample size = 2236
Patients aged ≥18 years undergoing elective surgery
Moderate and high risk for DVT
by the Department of Health VTE assessment tool

Assessed for eligibility  
\( n = 6000 \)

Approached  
\( n = 4500 \)

Consented  
\( n = 2236 \)

Baseline EQ5D

Computer randomisation  
\( n = 2236 \)

Pharmacological thromboprophylaxis
+ Graduated compression stockings  
\( n = 1118 \)

Pharmacological thromboprophylaxis alone  
\( n = 1118 \)

Exclusion
- Contraindications to LMWH
- Contraindications to GCS, including peripheral arterial disease, stroke patients, individuals undergoing lower limb surgery
- Documented or known thrombophilia or thrombogenic disorder
- Individuals requiring therapeutic anticoagulation
- Previous VTE
- Patients having IPC beyond theatre and recovery
- Patients requiring IVC filter
- Pregnancy
- Patients requiring extended thromboprophylaxis
- Cast or brace use
Follow-up

Pharmacological thromboprophylaxis + Graduated compression stockings  
\( n = 1118 \)

Pharmacological thromboprophylaxis alone  
\( n = 1118 \)

Surgery

Pharmacological thromboprophylaxis + Graduated compression stockings

Pharmacological thromboprophylaxis alone

Initial follow-up (1 week post-surgery or prior to discharge)
*Clinical assessment, proceeding to imaging if clinical suspicion, Patient VTE diary, EQ-5D*

Follow-up 14 – 21 days post-surgery
*Clinical assessment, *Duplex*, EQ-5D*

Follow-up 90 days post-surgery
*Telephone, online, SMS or face-to-face assessment, proceeding to imaging if clinical suspicion, EQ-5D*

Primary outcome – composite
- If clinical VTE confirmed on investigation at any point within 90 days, this will be recorded
  - Symptomatic DVT
  - Asymptomatic DVT identified by duplex
  - Imaging-confirmed symptomatic PE

Secondary outcome measures
- Quality of life – EQ-5D
- Compliance with stockings
- GEC-related lower limb complications (skin ulceration, ischaemia, …)
- Bleeding complications
- Allergic reactions to LMWH
Trial Progress

- To date 2475 patients screened
- 461 randomised (19% inclusion rate)
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Thank you