Graduated compression stockings in hip fractures

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ABSTRACT

INTRODUCTION Hip fractures are the most common cause of acute admissions to orthopaedics units and in the UK approximately 70,000–75,000 hip fractures occur annually. Hip fractures carry a significant risk of developing a venous thromboembolism. The National Institute for Health and Clinical Excellence (NICE) estimated that the risk of developing a venous thromboembolism in patients with hip fractures who do not receive thromboprophylaxis is 43%. In their recent guidelines, NICE recommended that combined mechanical and pharmacological thromboprophylaxis should be offered to patients undergoing hip fracture surgery and mechanical prophylaxis should be commenced at admission. The aim of this review was to search for available evidence that could support using graduated compression stockings combined with low molecular weight heparin (LMWH) in hip fracture patients.

METHODS NICE guidelines and the reference list of the guidance were reviewed and a thorough literature search was performed on main electronic databases (MEDLINE®, Embase™ and the Cochrane Library).

RESULTS A literature search was unable to find sufficient evidence to support the use of graduated compression stockings combined with LMWH in hip fracture settings. The guidelines are critically reviewed and the available evidence is discussed.

CONCLUSIONS The evidence supporting these recommendations is very limited and there is considerable concern regarding the safety and efficacy of the mechanical devices used in thromboprophylaxis. Further studies are needed urgently before specific guidelines can be agreed confidently for patients with hip fractures.
prophylaxis should be based on individual patient factors and could be any of the three following options: antiembo-
lisom stockings (AES)/graduated compression stockings
(GCS), foot impulse devices (FID) or intermittent pneumatic compression devices (IPCD). From a practical point of view, FID and IPCD can be class-
ified as one group while AES and GCS constitute a second.
IPCD and FID use an ‘active’ mechanism whereas GCS and
AES use a ‘passive’ method.2 In the NICE guidelines (and in
this review), the acronym GCS is used to refer to both AES
and GCS.
From our own observations, in practice, GCS are used
more commonly than IPCD/FID. A literature search did
not reveal any statistical evidence to support or disprove
this although Cohen et al estimated the use of GCS to be
70% for UK patients.8 Rajaganeshan et al conducted a na-
tional survey in the UK to determine the use of thrombo-
 prophylaxis in hip fracture patients.7 A questionnaire was
sent to 1,648 orthopaedic consultants and resulted in a 44%
(n=725) response rate. Of those who responded, 320 (58%)
used mechanical prophylaxis (mechanical prophylaxis
only or combined with pharmaco logical prophylaxis), 11
(5%) used stockings, 50 (9%) used foot/ankle pumps and
60 (19%) used Flowtron® boots (ArjoHuntleigh, Luton, UK).
The majority (96%, n=219) reported the use of mechanical
devices combined with other prophylactic methods but did
not provide further clarification on what combinations were
used. In addition, the response rate in this study was low
and it was conducted more than four years prior to the NICE
guidelines. It does not therefore reflect current practices.
Another reason to think that IPCD/FID are used less
commonly than GCS is that they raise concerns regarding
compliance and this has been reported to be a major issue.3,5
This is likely to be more problematic in the hip fracture pop-
ulation.
Based on this background and due to this lack of evi-
dence on best practice for VTE prophylaxis in hip fracture
patients, this review focused on this patient group. The pri-
mary aim was to search for evidence to support the use of
GCS in conjunction with LMWH in hip fracture patients.
The review also examined NICE guidelines and the gen-
eral available evidence for the use of GCS in hip fracture
patients.

Methods
The NICE VTE guidelines1 were reviewed for available
evidence on which the recommendations were based. The
reference list of the NICE guidelines was also searched for
relevant studies. A thorough literature search on the sub-
ject was undertaken in main electronic databases includ-
ing MEDLINE®, Embase™ and the Cochrane Library. The
keywords searched were ‘hip fracture’, ‘thromboprophyl-
xis’, ‘thromboembolism’, ‘pulmonary embolism’, ‘deep
vein thrombosis’, ‘mechanical prophylaxis’ and ‘graduated
compression stockings’. MeSH (Medical Subject Headings)
terms were also searched. The search strategy was not lim-
ited to time of publication or type of article but only papers
written in English were sought.

Results
The literature search did not identify any studies with a fo-
cus on hip fracture patients only comparing LMWH alone
with combined LMWH and GCS. However, one study was
mentioned in the NICE guidelines that compared hip frac-
ture patients who received fondaparinux with those who
received fondaparinux plus GCS.4 In the discussion below,
the focus is on the NICE guidelines and the available data on
which the guidance are based.

Discussion
Mechanical prophylaxis and hip fracture patients
NICE identified 50 RCTs that reported at least one of the
three main outcomes (DVT, pulmonary embolism and ma-
jor bleeding).7 Some of these RCTs investigated more than
two modalities of thromboprophylaxis. The data from most
of these RCTs had been extracted from systematic reviews
and, where applicable, the study was cited in the evidence
table for that review. RCTs covering patients with hip frac-
tures were included in six of the systematic reviews although
two studies included a mixed group of patients with both hip
fractures and elective hip replacements. Of the 50 RCTs, 25
were included in the network meta-analysis for DVT.
The quality of the included studies was evaluated and
the included RCTs were either appraised individually or
retrieved from systematic reviews that in turn had been appraised.2 However, 78% of the 25 RCTs included in the
meta-analysis were published before 1990. Consequently,
some of the surgical techniques cited are no longer in cur-
rent practice. In addition, 61% of the included RCTs had
fewer than 100 patients and, taken together, these factors
may severely limit the available evidence.
In the section of the guidelines entitled Summary of
Evidence for Mechanical and Pharmacological
Prophylaxis (pp148–155), there is no significant difference
noted between GCS combined with LMWH and LMWH
alone or between GCS combined with fondaparinux and
fondaparinux alone, in the outcome of DVT and pulmonary
embolism, in all available evidence and across all patient
groups (medical, surgical and trauma patients).2 GCS are,
however, linked to a significant increase in adverse events
in stroke patients, such as skin breaks, ulcers, blisters and
skin necrosis.5

In a multicentre, outcome blinded RCT, Dennis et al
allocated 2,038 stroke patients, recruited internationally
from 64 centres, to routine care plus thigh-length GCS or
routine care avoiding the use of GCS.7 The results showed
that thigh-length GCS did not result in a statistically signifi-
cant difference in the measured outcome (symptomatic or
asymptomatic DVT in the popliteal or femoral veins). In fact,
complications (eg ulcers, blisters and skin breaks) were sig-
nificantly higher in patients allocated to the GCS group even
though patients with peripheral vascular disease or diabe-
tes, those who had sensory neuropathy or those for whom
the responsible clinician or nurse judged that GCS might
cause a skin break were excluded.
NICE argued that these results were found in a special

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likely to be transferrable to other populations. However, it can also be argued that the safety of GCS in a hip fracture population has not been proven. No similar studies on hip fracture patients were identified by the guidelines or could be found through a literature search. Additionally, none of the 50 RCTs reviewed by NICE that investigated the different methods of thromboprophylaxis compared LMWH with combined mechanical and pharmacological prophylaxis following hip fracture surgery.

Previous randomised studies have reported a significant reduction in post-operative thrombosis associated with compression stockings. Ohlund et al conducted a trial of 65 patients who received mixed elective hip surgery and Fredin et al undertook a study of 150 patients admitted for elective total hip arthroplasty. Both groups in both studies received dextran as their primary thromboprophylaxis. It is very likely that the small sample size contributed significantly to the results of these studies. In addition, the use of dextran is now an outdated intervention for thromboprophylaxis.

In a larger and more recent multicentre randomised trial on the use of GCS in association with hip surgery, 400 patients who received fondaparinux were compared with 395 patients who received fondaparinux plus GCS. No difference was observed in the prevalence of VTE between the two groups. Despite careful selection, 2% of the patients developed complications related to the use of stockings. Although the study had a large sample size, was well randomised and the level of compliance was high, it is difficult to generalise the results for hip fracture patients. The population of the study was a mix of elective and hip fracture cases with only about 5% having a fractured hip. Hip fracture patients are usually fragile and elderly in comparison with fit arthroplasty patients admitted for surgery electively. In a systematic review of 31 trials, Handoll et al did not find any randomised trial testing the use of GCS in hip fracture patients.

In addition to safety concerns regarding GCS, there is some survey evidence that they are associated with reduced quality of life (eg disutility and discomfort). One of the disadvantages of ultrasonography is that it appears to be operator dependent and there are discrepancies between readers. The burden of proof should therefore be on the intervention (ie mechanical prophylaxis) and due to the lack of evidence describing their benefit and the presence of concerns regarding their potential harm, it is questionable as to whether applying the guidelines of mechanical prophylaxis to hip fracture patients should be accepted or whether further investigations and studies should be undertaken to provide evidence for their use in improving patient outcomes.

The use of surrogate endpoints
It has been a routine practice for trials examining the clinical effectiveness of thromboprophylaxis to set an outcome of asymptomatic and symptomatic DVTs, and detection of asymptomatic DVT in most of the research on thromboprophylaxis in orthopaedic surgery has been based on venography. However, the safety and efficacy of venography in detecting asymptomatic DVT has been widely questioned. First, venography is invasive, uncomfortable and possibly thrombogenic, and second, studies have shown that anticoagulant prophylaxis may delay the peak onset of DVT. Sikorski et al found that the peak onset of DVT in untreated post-total hip replacement patients was on the fourth day, a second smaller incidence peak occurred on day 15 and the risk of DVT was over by day 17. In contrast, the peak incidence in the group treated with heparin was on day 6 and the risk of thrombosis continued to day 18 or beyond.

A single venogram can only measure prevalence rather than incidence and it will not detect early thrombi or those that occur later. Additionally, repeating venography on several occasions to reduce this discrepancy between prevalence and incidence is impractical. However, venography does have some advantages. It is simple and easy to perform, and it has also been argued to be more sensitive than non-invasive methods such as ultrasonography for the diagnosis of asymptomatic DVT.

Ultrasonography has been suggested as an alternative non-invasive and repeatable diagnostic tool. Nevertheless, its accuracy and sensitivity have been questioned, especially for detecting asymptomatic DVT. Complete compression ultrasonography and colour-flow Doppler ultrasonography have been trialled for this purpose. Several studies have compared these two modalities of ultrasonography or ultrasonography and venography but all these studies were carried out on elective arthroplasty patients.

A literature search was unable to find sufficient data for similar studies but in a hip fracture setting. Mitra et al found no correlation between clinical symptoms and venography findings for post-operative screening in hip fracture patients. The limitation of this study was clear: a very small number of included patients (n=72). Nevertheless, the results are variable and no definitive conclusions could be drawn.

One of the disadvantages of ultrasonography is that it appears to be operator dependent and there are discrepancies between readers. These factors have probably contributed to the discrepancies in the findings between the aforementioned studies. In some of the literature, ultrasonography as a diagnostic tool for DVT is considered to be the imaging method of choice for patients with clinically suspected DVT but its use for post-operative screening for asymptomatic DVT has not been specifically verified.

The timing of screening is another area of disagreement and variable target days have been investigated by different researchers. Ciccone et al performed ultrasonography and venography on the fifth to seventh day post-operatively while in the study by Leutz and Stauffer ultrasonography and venography were performed 5–9 days after surgery and Schellong et al performed venography 5–9 days after surgery and ultrasonography within 24 hours after venography. This choice of timing is based on convenience rather than epidemiological or haematological evidence since this period is the typical duration of the hospital stay following joint arthroplasty.

The dilemma regarding setting asymptomatic thromboembolism as an outcome does not end at what screening tool should be used and when the screening should be
carried out as it is not fully clear whether one or both legs should be imaged. There are very limited clinical data to support the use of bilateral ultrasonography in patients with suspected unilateral DVT.\footnote{28} In post-operative surveillance, some researchers have favoured screening the operated leg only\footnote{25} but many other authors have suggested that bilateral venography is crucial. More recently, Warwick and Samama have reported that up to 20\% of post-operative DVT occurs in the contralateral leg.\footnote{17} In a systematic review of prospective studies that gave DVT as the primary outcome based on bilateral venography following surgery for elective hip or knee arthroplasty or hip fracture, the risk of isolated DVT in the non-operated leg was estimated to be 4–5\%.\footnote{28} The authors concluded that performing venography on both legs reduced the risk of missing the diagnosis and improved the efficacy of the study.

Previous consensus guidelines have been based on the meta-analysis of large numbers of small trials that have used surrogate endpoints such as venography, ultrasonography and lung scanning,\footnote{26,27} and most published trials are limited, and there is considerable concern regarding the meta-analysis based on a large number of studies with a small number of patients and whether the results reflect clinically significant events.\footnote{25,28,29}

Recording the outcome of asymptomatic DVT is not without its advantages. Asymptomatic thrombi occur much more often than those that are clinically symptomatic. Therefore, surrogate endpoints are used because they provide statistical conclusions that can be reached via a smaller number of patients.\footnote{16} Lee et al found that the use of bilateral venography reduces the required sample size by 16–25\% compared with ipsilateral venography.\footnote{17}

There are significant concerns regarding the findings of these studies and their use in the clinical guidelines published by NICE.\footnote{2} In clinical medicine, physicians and surgeons should be interested in clinical outcomes\footnote{3} and it is a matter for debate whether clinical practice should be based on surrogate endpoint findings.

Conclusions

In the NICE guidance published in 2010, the use of a combination of mechanical and pharmacological prophylaxis in hip fracture patients was recommended (unless there is contraindication).\footnote{2} The evidence that supports this is very limited, and there is considerable concern regarding the safety and efficacy of the mechanical devices of VTE prophylaxis. Researchers should be encouraged to further explore this area, which is lacking in good quality evidence, and it is to be hoped that NICE will consider this issue in the future review of the guidance.

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