The New Ropanasuri Journal of Surgery

Volume 7 | Number 1 Article 6

6-23-2022

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Recommended Citation

Pratama, Dedy and Simatupang, Satria M.H (2022) "Graduated Compression Stockings for Deep Vein Thrombosis prevention in Surgical Patients: A Systematic Review," *The New Ropanasuri Journal of Surgery*: Vol. 7: No. 1, Article 6.
DOI: 10.7454/nrjs.v7i1.1113
Available at: https://scholarhub.ui.ac.id/nrjs/vol7/iss1/6

The New Ropanasuri Journal of Surgery
OPEN ACCESS
Published by Department of Surgery
Faculty of Medicine, Universitas Indonesia

Graduated Compression Stockings for Deep Vein Thrombosis prevention in Surgical Patients: A Systematic Review

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Corresponding author: dedygpratama@yahoo.com Received: 27/Dec/2021 Accepted: 18/May/2022 Published: 23/Jun/2022
Website: https://scholarhub.ui.ac.id/nrjs/ DOI:10.7454/nrjs.v7i1.1113

Abstract

Introduction. Oral anticoagulant therapy is commonly used to prevent deep vein thrombosis (DVT). However, it might increase the risk of intraoperative and postoperative bleeding. Graduated compression stockings (GCS) reduced DVT risk, but there is a lack of supporting evidence. Thus, the study aimed to find the efficacy of GCS compared to the pharmacological method in high-risk surgical patients.
Method. Literature search proceeded in Cochrane, ClinicalKey, and PubMed. Using keywords graduated compression stockings" or "mechanic" or mechanical") and ("pharmacologic" or "oral anticoagulants" or "NOAC") and "comparison" and "prophylaxis" and ("DVT" or "deep vein thrombosis) and ("surgery" or "surgical").
Results. There were six articles reviewed (27,966 participants). The analysis focused on follow-up, diagnostic method, GCS application days, thromboprophylaxis baseline used, and outcomes, i.e., DVT and pulmonary embolism. No statistically significant clinical advantage was found in surgical patients using the mechanical method of GCS for DVT prophylaxis over the pharmacological method.
Conclusion. No significant clinical advantage of using the GCS for DVT prophylaxis over the pharmacological method but preventing intraoperative and postoperative bleeding. However, the efficacy of GCS remains an issue to be evaluated, as recently supported by insufficient data. However, GCS implementation as a prophylactic method in surgical patients with a high risk of DVT contraindications for pharmacological prophylaxis is safe.

Keywords: graduated compression stocking, deep vein thrombosis, oral anticoagulants

Introduction

Deep vein thrombosis (DVT) is mainly found in the lower extremities and pelvic, leading to swelling and painfully affected extremities. If unmanaged, DVT might lead to a complete resolution of the block or death due to pulmonary embolism.[1] IDENTIA registry data 2020 showed, in Indonesia, that of 360 subjects with acute illness at high risk of DVT over 40 years, the incidence of DVT was 37.1–40.3%, with a mean Wells score of 3 and an average of laying down of nine days.[1] Meanwhile, NICE data 2010 showed the incidence of DVT in surgical and nonsurgical patients was 29% and 24%, respectively.[2]
Some preventive measures have been recommended, both pharmacological and mechanical. Pharmacologically, oral anticoagulant administration is the typical treatment applied for prevention purposes. However, intraoperative and postoperative bleeding in surgical patients is an adverse effect that should be noted following this treatment. Mechanical graduated compression stockings (GCS) have reduced the risk of DVT. Unfortunately, studies focused on this method remain minimal. Therefore, this study aimed to find the most decisive evidence showing its efficacy.

Method

A systematic review study was conducted following preferred reporting items for systematic review and meta-analysis protocols (PRISMA). The literature search proceeded on Cochrane, PubMed, and ClinicalKey using keywords "graduated compression stockings" or "mechanic" or mechanical" and "pharmacologic" or "oral anticoagulants" or "NOAC"

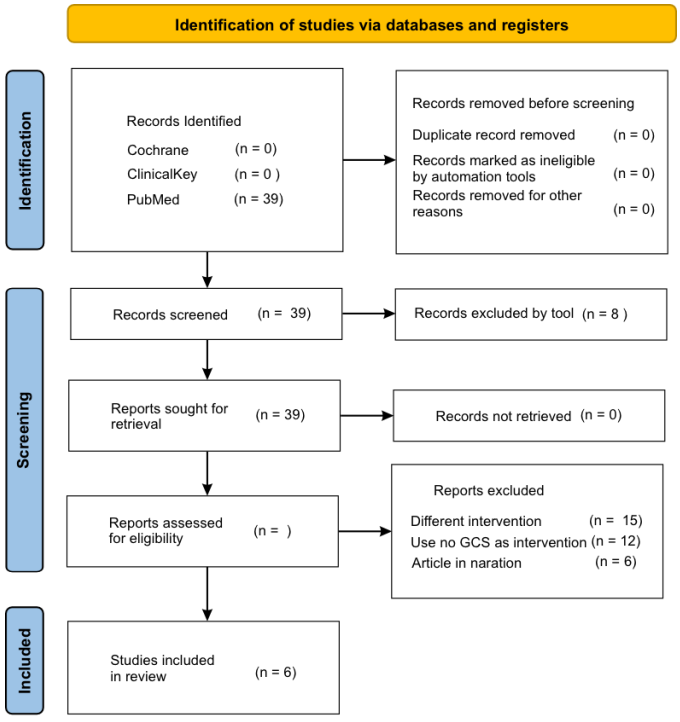

Figure 1. Flow chart in literature search following PRISMA 2020.

and "comparison" and "prophylaxis" and "DVT" or "deep vein thrombosis and "surgery" or "surgical". All articles focused on GCS as the mechanical prevention for DVT compared to pharmacological measures in high-risk surgical patients. Studies published in English over the past ten years were included in this study. While the studies focused solely on (oral anticoagulants), correspondence studies, studies that did have the outcome, and studies with unavailable full text were excluded. Selected articles were screened and appraised for the study design, samples, validation of results, etc., to find the strength of evidence. The analysis was focused on DVT incidence, diagnostic method, GCS duration, and follow-up.

Results

In the literature search, 39 articles were found from PubMed. Six articles were included after the screening, including four randomized controlled trials and two case-control studies (see figure 1). Of these articles, only an article definitively compared GCS with pharmacological measures. Other articles investigated the efficacy of GCS as an adjunct intervention to pharmacological prophylaxis. These studies were listed in tables 1 and 2, including the level of evidence.

Discussion

Six articles with 27,966 participants from six different centers were included. Five studies by Chin, Fuji, Nam, Shalhoub, and Suna showed the incidence of 0.1–0.8%, with p >0.01.[3-6] Four articles (Chin, Fuji, Nam, and Suna) reported the incidence of pulmonary embolism of 0.1–0.7%, which was not significantly associated with DVT (p >0.01).[3–5,7] With this low incidence and limited studies with relatively small samples, it is difficult to conclude GCS efficacy in preventing DVT in surgical patients, even though Chin (2010) found that using GCS as prophylaxis was more effective than those not.[3] However, the NICE guidelines recommend using GCS to prevent DVT in hospitalized patients who cannot be treated using pharmacological prophylaxis.[2]

Studies showed that intraoperative and postoperative bleeding is a major factor in discontinuing pharmacologic prophylaxis in surgical patients at high risk of DVT. This is in line with the study by Sang et al., 2018, who showed adverse effects of pharmacological prophylaxis, such as bruising at the injection site, hematoma, vaginal bleeding, bleeding from the drain, and hematuria.[8] Participants included in this study were patients who underwent digestive, oncology, gynecology, orthopedic, and general surgery, thus providing good evidence when applied to this population. GCS efficacy is evaluated between days seven and fourteen as reported in four articles (Chin, Fuji, Nam, and Suna).[3–5,7] Sweetland showed that the risk of developing DVT was within six weeks postoperatively.[9] Thus, the short-term evaluation indicates that these four articles did not cover a sufficient period of evaluating the risk manifests and failed to show the prophylactic effect of DVT in surgical patients. Furthermore, none of the articles agreed on how long GCS to be applied, both pre– and postoperatively (whether to continue use until mobilization or until a clinic follow-up visit). This aspect is essential because DVT and pulmonary embolism can occur after the patient is discharged or in an outpatient setting.

Most studies carry out duplex ultrasonography (USG) to establish DVT. This examination is a commonly used method for diagnosing DVT as it is inexpensive and easy to proceed with. While as a standard diagnostic method recommended by the 2018 American Heart Association (AHA), duplex ultrasound is very operator-dependent.[10] Although the basic principle of using Ultrasound is clear, the articles do not explain the details. It is interesting to note that minimal new studies – particularly in the last ten years – directly compare mechanical and pharmacological prophylaxis focused on the outcomes of both DVT and pulmonary embolism.[11–17]

Recommendations and guidelines should be developed to address the criticism regarding the quality evidence from previous studies, which was mainly secondary. RCT is the ideal design to find the efficacy of such an intervention. However, it is realized that RCT is challenging since treating using a placebo for mechanical prophylaxis is impossible.[17] Therefore, most RCT studies were conducted using positive clinical trials using accepted general pharmacological prophylaxis, then adding GCS in the treatment group to assess the effectiveness of GCS use, resulting in a study of the relative efficacy of GCS. The challenge is that the data generated by comparing the two existing prophylactic methods will likely result in a low incidence of both DVT and pulmonary embolism in both groups, as both interventions are equally effective. When a study shows no statistically clear difference, it does not indicate that the role of GCS as a prophylactic method is not significant, but it is likely that the sample size used in this study is still too small. The danger is that this can lead to wrong conclusions and poor clinical decisions.[11–17] Another ambiguous conclusion from studies with control groups receiving pharmacological prophylaxis is that the prophylactic effect achieved and the degree of side effects avoided would require a combination of the two if the desired outcome is achieved. This research method has difficulties, namely the possibility that the GCS prophylactic method alone does not affect because the prophylactic effectiveness comes from the baseline treatment. Therefore, research in this form must be careful in concluding because it has an ambiguous clinical meaning.[11]Patients who do not receive a GCS may quickly realize they are not receiving active therapy.[11–17]

Another challenge was standardizing the application because the technique is not pressure-controlled by design but operator-dependent. Also, the material used and the anatomy of the patient's foot are immensely varied. Another critical issue is rationalizing the expected primary effect, which is to prevent thrombus formation in deep veins. Finding objective measures in the assessment is not easy since many factors play a role in venous flow.[11–17] It is necessary to conduct trials to evaluate the efficacy with a more significant effect size. Along with the development of science and technology, there are possibilities to proceed with future studies focused on comparing GCS with oral anticoagulants for prophylaxis purposes. In addition, the ideal compression with individual adjustment to the change in deep venous blood flow can be objectively evaluated to obtain the best mechanical effect.[11–17]

The review failed to find the research questions due to insufficient data; studies focused on mechanical and pharmacological prophylaxis, referred to as minimal. These studies used thromboprophylaxis as the baseline, which may lead to bias in evaluating GCS efficacy. Further, the application of GCS in these studies considerably varied between 7-14 days to six weeks postoperatively, unable to demonstrate the true magnitude of the prophylactic effect of DVT in surgical patients as DVT and pulmonary embolization may occur after hospital discharge.

Conclusions

No significant clinical advantage of using the GCS for DVT prophylaxis over the pharmacological method but preventing intraoperative and postoperative bleeding. However, the efficacy of GCS remains an issue to be evaluated, as recently supported by insufficient data. However, GCS implementation as a prophylactic method in surgical patients with a high-risk of DVT who have contraindications for pharmacological prophylaxis is safe.

Table 1. Study characteristics (part A)

Author, Year	Country	Study Design	Total participants	Age (*mean* ± SD)	Gender	Diagnostic Method of DVT	*Follow-up period* (days/month)	Statistical Analysis	Level of evidence*
Chin, 2010[3]	Singapore	Multicentered RCT	440	65 ± 22	Male and female	USG duplex	One month	Chi-square test	2
Fuji, 20164	Japan	Multicentered RCT	201	1. Control group with edoxaban: 70.9 ±7.9 2. Control group with enoxaparin: 71.7 ±7.8 3. Treatment group with edoxaban: 73.5 ±6.1 4. Treatment group with enoxaparin: 73.2 ±7.0	Male and female	Venography	25 - 35 days	Chi-square test	2
Nam, 20175	South Korea	Case-control	539	1. Control group: 82.2 ± 6.3 2. Treatment group: 82.0 ± 5.6	Male and female	CT angiography	One month	Chi-square test	4
Sang, 20188	China	Multicentered RCT	625	1. Group A: 54.2 ± 9.4 2. Group B: 54.7 ± 11 3. Group C: 52.6 ± 9.9 4. Group D: 53.5 ± 10.5	Female	USG duplex	Six months	Chi-square test, T-test, Fisher exact test	2
Suna, 20207	German	Case-control	24,273	1. Control group: 2. 61.8 ± 18.7 3. Treatment group: 61.6 ± 18.4	Male and female	USG duplex	Perioperative during January 2006-January 2011	T-test, Fisher exact test	4
Shalhoub,	England	Multicentered RCT	1,888	1. Control group: 59.3 ± 15.2 2. Treatment group: 58.1 ± 14.9	Male and female	USG duplex	14-21, and 90 postoperative days	Generalized linear modeling, non-inferiority	2

*levels of evidence according to Center of Evidence-Based Medicine University of Oxford 2011, CT: Computed Tomography, RCT: Randomized Controlled Trial, USG: Ultrasonography

Table 2. Study characteristics (part B)

Author, Year	Inclusion Criteria	Exclusion Criteria	Disciplines	Control	Treatment	GCS Application (days)	Baseline Thromboprophylaxis	Outcomes		
								DVT	PE	Others
Chin, 2010[3]	Patients undergoing elective surgery for total knee arthroplasty without a predisposition to VTE	History of using anticoagulant/aspirin, previous PE and DVT, bleeding, stroke within three months, allergy to heparin	Orthopedic surgery	110	110	5-7 days	Not given	Prevalence: Control group 22% vs GCS 13%, p = 0.119 Control group 22% IPC 8%, p = 0.032 Control group 22%	1% vs. 1% p = 0.571	Participants were divided into four groups: 1. Without prophylaxis, 1. GCS only 2. IPC only 3. LMWH only
Fuji, 2016[4]	Not mentioned	Patients who have used IPC	Orthopedic surgery	100	101	11-14 days	Edoxaban or enoxaparin	Asymptomatic: Control group with edoxaban 3/52 (5.8%) Control group with enoxaparin 10/48 (20.8%) Treatment group with edoxaban 2/53 (3.8%) Treatment group with enoxaparin 4/48 (8.4%)	No patient had PE	No data

Table 2. Study characteristics (part B) cont.

Author, Year	Inclusion Criteria	Exclusion Criteria	Disciplines	Control	Treatment	GCS Application (days)	Baseline Thromboprophylaxis	Outcomes		
Nam, 2017[5]	Patients >70 years of age undergoing surgery for control fracture of the femoral neck or intertrochanteric fracture	History of laying down before the injury Previous VTE, Using warfarin	Orthopedic (hip fracture surgery)	404	135	Starting 18 months before surgery	Aspirin, *clopidogrel*, LMWH	Symptomatic: Control group 30/404 (7.4%) vs treatment group 3/135 (2.2%) with OR 0.28 (95% CI) p = 0.042	Control group 15/404 (3.7%) vs Treatment group 2/135 (1.5%) with OR 0.39 (95% CI) p = 0.223	No data
Sang, 2018[8]	Age > 18 years, have postoperative risk factors for VTE willing to sign the informed consent form	Using VTE prophylaxis before the study	gynecology surgery	0	Group A: 159 Group B:157 Group C: 153 Group D: 156	Since arriving in the operating room or 2 hours postoperatively Furthermore, it is used for 16 hours every day to 7 postoperative days	Patients were divided into four groups: A. GCS only B. GCS + LMWH C. GCS+IPC D. GCS+IPC+LMWH	Of the 625 patients, 32 had DVT: Group A: 14 (8.8%), Group B: 6 (3.8%), Group C: 8 (5.2%), Group D: 4 (2.6%). Overall incidence (32/625) 5.1%	Of the 625patients, 12 with PE: Group A: 7 (4.4%), Group B: 1 (0.64%), Group C: 3 (1.96%), Group D: 1 (0.64%). Overall incidence (12/625) 1.9%	Observation on 7th postop days, no major bleeding and heparin-induced thrombocytopenia Group A no bleeding. Group B 13/28 with bruising at the injection site, 6//28 with hematoma, and 5/28 with vaginal bleeding.
Suna, 2020[7]	Surgical patients between January 2006 January 2011	Age <18 years Has contraindications for GCS: PAD, PAOD.	General and orthopedic surgery	12612	11661	During the perioperative period	LMWH	Symptomatic: control group 17 (0.1%) vs treatment group 22 (0.19%) RR 0.715 p >0.05 95%CI (0.380-1.345)	Symptomatic: Control group 19(0.2%) vs treatment group 29 (0.2%) with RR 0.795 p >0.05 (95%CI 0.632-1.000)	
Shalhoub 2020[6]	Inpatient elective surgery patients with moderate to high risk of VTE, able to give informed consent to participate in the study, over 18 years of age	Contraindicated to LMWH, GCS (PAD, stroke, individuals undergoing lower limb surgery), thrombophilia, previous VTE, pregnancy	General surgery (Upper and lower gastrointestinal tract)	948	940	During hospitalization up to 90 days postoperatively	LMWH	Symptomatic: Control group 0.2% vs treatment group 0.1% Asymptomatic: Control group 1.5% vs treatment group 1.4% VTE: Control group 16/937 (1.7%) vs treatment group 13/921 (1.4%) (risk difference 0.30% with 95%CI 0.65%–1.26% p <0.01 for non-inferiority	Control group 2/937 (0.2%) vs treatment group 1/921 (0.1%)	No data

CT: Computed Tomography, DVT: Deep Vein Thrombosis, PE: Pulmonary Emboli, GI: Gastrointestinal, IPC: Intermittent Pneumatic Compression, LMWH: Low Molecular Weight Heparin, PAD: Peripheral Arterial Disease, PAOD: Peripheral Arterial Occlusive Disease, RCT: Randomized Controlled Trial, USG: Ultrasonography

Disclosure

Authors declare no conflict of interest

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