Mini Review

Interventional Cardiology

The effect of graduated elastic compression stockings to prevent post-thrombotic syndrome after deep vein thrombosis

Abstract

The ability of graduated elastic compression stockings to reduce the risk of post-thrombotic syndrome after deep vein thrombosis has been questioned for many years. This mini review presents noteworthy results of recent years' studies and highlights unresolved issues.

Keywords: Deep vein thrombosis • Post-thrombotic syndrome • Elastic compression stockings • Hyperpigmentation • Lipodermatosclerosis

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Received date: 05-Nov-2024, Manuscript No. FMIC-24-151760;
Editor assigned: 07-Nov-2024, PreQC No. FMIC-24-151760 (PQ);
Reviewed date: 21-Nov-2024, QC No. FMIC-24-151760;
Revised date: 28-Nov-2024, Manuscript No. FMIC-24-151760 (R);
Published date: 05-Dec-2024, DOI: 10.37532/1755-5310.2024.16(5).924

Introduction

Since the large randomized Swedish Orveito-X (SOX) trial a decade ago found that graduated Elastic Compression Stockings (ECS) did not prevent Post Thrombotic Syndrome (PTS) after a first proximal Deep Vein Thrombosis (DVT), the use of ECS after DVT has been questioned [1]. The results were in contrast to the first randomized study by Brandjes et al., where it was found that the use of ECS led to a significant reduction in the risk of developing PTS after proximal DVT by approximately 50% [2]. The results of the SOX trial influenced the attitude towards the use of ECS after DVT, as guidelines in Canada, the United States and the United Kingdom stopped recommending the use of ECS after DVT.

Common symptoms of PTS are chronic swelling and heaviness in the leg. In more severe cases, pain, venous claudication and irreversible skin changes such as venous ectasia, hyperpigmentation, lipodermatosclerosis and venous ulceration may occur. It is estimated that mild-moderate and severe PTS after proximal DVT occurs in 40%-50% and 5%-10%, respectively. We recently looked at the evidence that ECS can prevent or reduce these lifelong troublesome sequelae of DVT [3].

The aim of this review is to report in which situations there is evidence for a significant effect of ECS and areas where evidence is still lacking.

Literature Review

After the SOX trial, six meta-analyses were published over the next couple of years. Half of the meta-analyses concluded that there was no effect of ECS as the results of the large SOX trial dominated the overall result [4-6]. Others found, by the inclusion of various smaller studies, that ECS might prevent the development of PTS, but due to the heterogeneity between the studies, it was considered that further evidence was needed [7-9]. In some of the studies, patients were randomized to ECS versus no ECS several months after DVT and other meta-analyses included studies of compression bandages, patients with isolated distal DVT and studies without a control group.

Discussion

These meta-analyses had no particular influence on the attitude towards the use of ECS for the prevention of PTS. It was not until Yang et al., in a randomized study of ECS versus no ECS comprising 232 patients with a first proximal DVT found a significantly lower incidence of PTS in patients in the ECS group than in the control group (42.0% versus 57.8%. RR: 0.73; 95% CI: 0.55-0.97; p=0.024) that there was renewed confidence in the prophylactic effect of ECS [10]. They also found a higher quality of life and less severity of symptoms among ECS users (VEINESQoL scores: 63.7 ± 4.6 vs. 60.6 ± 6.9; p<.001; VEINESSym scores, 45.8 ± 5.1 vs. 43.8 ± 6.1; p=0.014).

Their results were supported by a study by Prandoni et al., comparing the incidence of PTS among 511 patients who, for at least two years after proximal DVT, had used ECS for at least 70% of the day, with 350 patients who used the stocking less often or not at all [11]. After a mean follow-up of 5 years, 31.7% of patients with extensive use of ECS developed PTS versus 50.6% in the group of patients who used ECS less often (HR: 0.64; 95% CI: 0.51-0.79; p<0.001).

Prandoni's study also provided an idea as to why the SOX trial had failed to show a PTS-preventive effect of ECS after proximal DVT. Probably, the reduced adherence to the use of ECS was the main reason for the negative outcome of the study. In the SOX trial, patients were considered "users of ECS" if they had used ECS for just 3 days a week since the last check-up. This is far less than in the previous studies and in the above-mentioned study by Prandoni et al. [11].

Another problem in the SOX trial was that it was not ensured that the fit of the supplied ESCs was correct. During hospitalization, the patients were instructed on how to use ESC. After randomization, the patients were sent ESC or placebo stockings, but they were not visited by a home nurse to check that the fit was correct and at later outpatient check-ups they had to appear without stockings for reasons of study blinding. Inadequate instruction of the patients and poor fit of the ECS may be another reason for the low adherence to ECS use.

Due to these weaknesses of the SOX trial, we excluded this study from our meta-analysis. We only included studies that met the following criteria:

- Patients with proximal DVT
- Use of ECS from early after diagnosis of DVT in the treatment group
- Use of ECS for at least 2 years after DVT in the treatment group
- Use of ECS for at least 4 days a week in the treatment group
- Less frequent or no use of ECS in the control group

Four studies met these criteria and meta-analysis of these studies suggests that the use of ECS significantly reduces the incidence of both mild-moderate PTS (Odds Ratio (OR) 0.48; 95% Confidence Interval (CI) 0.36-0.63) and severe PTS (OR 0.44; 95% CI 0.28-0.58). None of the studies found any effect of ECS on the incidence of recurrence of DVT.

Although it now seems certain that daily use of ECS can reduce the risk of PTS after proximal DVT, there are still some unsettled issues:

Should ECS be used immediately after diagnosis?

Early start of application of ECS is suggested as it has been shown that the use of ECS immediately after diagnosis of DVT more often leads to recanalization of thrombosed veins than if the start of ECS use occurs 2 weeks later [12].

Is ECS indicated in isolated distal DVT?

Isolated distal DVT is the most common form of DVT. The risk of PTS after isolated distal DVT is generally lower than after proximal DVT. There are, however, a minority who develop severe PTS [13]. Therefore, the use of ECS should be considered in patients admitted with isolated distal DVT accompanied by marked symptoms.

Should ECS always be used for at least 2 years?

In the Dutch-Italian IDEAL DVT study, 865 patients with acute proximal DVT were randomized to treatment with ECS for 2 years and individualized treatment for 6-12 months. The individualized group stopped using ECS if no signs of PTS were found at the current and previous check-up in the outpatient clinic after 3, 6 and 12 months. ECS therapy was stopped after 6 months in 25% and after 12 months in a further 11%. No difference was found between the incidence of PTS after individualized treatment (29%) and standard 2-year treatment (28%) (OR 1.06; 95% CI 0.78-1.44) [14].

Is thigh-length ECS better than below-knee ECS?

The effect of thigh-length and below-knee ECS was compared in a randomized study comprising 267 patients with a first episode of proximal DVT [15]. ECS had to be used during the day for a period of 2 years and the patients were followed for up to 3 years. There was no significant difference between the incidence of PTS after wearing thigh-length ECS (32.6%) and below-knee ECS (35.6%) (adjusted HR 0.93; 95% CI 0.62-1.41). Although thigh-length ECSs is more difficult to use, some patients with severe thigh swelling may prefer these stockings. For these patients, a personalized choice of stockings should be considered.

Are class II ECSs as effective as class III ECSs?

It has so far been standard to use ECS pressure class III with an ankle pressure of 30-40 mmHg for the prevention of PTS after DVT. The randomized CELEST trial studied the ability of 25 mmHg versus 35 mmHg ECS to prevent PTS after a first proximal DVT [16]. PTS occurred in 25/154 (29%) in the 25 mmHg group and 52/148 (35%) in the 35 mmHg group (RR 0.83; 95% CI 0.60-1.16). ECS with an ankle pressure of 30-40 mmHg is still considered the standard, but if a patient has difficulty using this, it can lead to low adherence. In these cases, ECS 25 mmHg may be a useful alternative. More widespread use of ECS 25 mmHg rather than the standard ECS of 30-40 mmHg should await the results of further studies.

Conclusion

After several years of doubt about whether the use of ECS after proximal DVT can reduce the risk of developing PTS, we can now state that this is most likely the case. As described above, there are still areas where the effect of ECS is unsettled. In addition, the importance of ECS after endovascular recanalization of iliofemoral veins has not yet been established. Studies in this area are warranted.

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