

The Effects of Body Mass Index on Efficacy of Intermittent Pneumatic Compression

Vücut Kitle İndeksinin Aralıklı Pnömatik Kompresyon Etkililiği Üzerindeki Etkileri

© Merve Ekşioğlu¹, © Arda Demirkan², © Ahmet Burak Oğuz³, © Ömer Arda Çetinkaya², © Behnan Gülünay⁴, © Müge Günalp Eneyli³

¹Yeditepe University Faculty of Medicine, Department of Emergency Medicine, İstanbul, Turkey

²Ankara University School of Medicine, Department of General Surgery, Ankara, Turkey

³Ankara University School of Medicine, Department of Emergency Medicine, Ankara, Turkey

⁴Sivas Numune Hospital, Clinic of Emergency Medicine, Sivas, Turkey

Abstract

Objectives: The aim of our study was to compare the efficacy of intermittent pneumatic compression on venous hemodynamics in individuals with different body mass indexes (BMIs).

Materials and Methods: The study included a total of 48 healthy volunteers. The participants were classified into three groups according to their BMIs as <24.9 kg/m² (group I), 25-29.9 kg/m² (group II), and >30 kg/m² (group III). The measurements of pulse, arterial blood pressure and oxygen saturation were made, and venous ultrasonography was performed by the investigator. The measurements were repeated at the 30th minute of intermittent pneumatic compression. Vena femoralis communis (common femoral vein) (VFC) vein flow dynamics were evaluated 1-1.5 cm proximal to the junction of the VFC and great saphenous vein.

Results: The increases observed in the peak systolic flow rates of both right and left VFC in groups I and II were found to be significantly higher compared to those observed in group III at the 30th minute of intermittent pneumatic compression application. (p<0.001, p=0.012, and p=0.049, respectively)

Conclusion: We demonstrated that intermittent pneumatic compression application increased the femoral venous flow; however, this effect changed among individuals with different BMIs. We believe that BMI should be considered as an independent risk factor in patients for whom venous thromboembolism prophylaxis has been planned, which is frequently encountered in emergency units, and that providing the same effect in individuals with different physical properties is important in planning the prophylaxis.

Key Words: Venous Thromboembolism, Pneumatic Compression, Femoral Vein, Ultrasonography

Öz

Amaç: Çalışmamız aralıklı pnömatik kompresyonun, farklı vücut kitle indeksine (VKİ) sahip bireylerde venöz hemodinamiye olan etkilerinin karşılaştırılmasını amaçlamaktadır.

Gereç ve Yöntem: Çalışmaya sağlıklı gönüllülerden olmak üzere toplam 48 birey dahil edildi. Çalışmaya alınan gönüllüler, hesaplanan VKİ'leri <24,9 kg/m² olan (grup I), 25-29,9 kg/m² arasında olan (grup II) ve >30 kg/m² (grup III) olan olmak üzere üç gruba ayrıldı. Nabız, arteriyel kan basıncı ile oksijen saturasyonu ölçümleri ve venöz ultasonografi incelemeleri çalışmayı yürüten araştırmacı tarafından yapıldı. Aralıklı pnömatik kompresyon uygulamasının 30. dakikasında ölçümler tekrarlandı. Vena femoralis communis (ortak femoral ven) (VFC) çapı ve venöz akım dinamiği, VFC'nin büyük safen venle bileşkesinin 1-1,5 cm proksimalinden değerlendirildi.

Bulgular: Grup I ve grup II'de olan bireylerin, aralıklı pnömatik kompresyon uygulamasının 30. dakikasında, sağ ve sol VFC tepe sistolik akım hızlarının artışı, grup III'de olan bireylerin, sağ ve sol vena femoralis communis tepe sistolik akım hızlarının artışına oranla istatistiksel olarak anlamlı yüksek bulundu (sırasıyla, p<0,001, p=0,012, p=0,049).

Sonuç: Aralıklı pnömatik kompresyon uygulamasının femoral venöz akışı artırdığını; ancak bu etkinin farklı VKİ'lere sahip bireyler arasında değiştiğini gösterdik. VKİ'nin, acil servislere sıklıkla karşılaşılan, venöz tromboembolizm profilaksisi planlanan hastalar için bağımsız bir risk

Address for Correspondence/Yazışma Adresi: Spc. Dr. Merve Ekşioğlu, MD,
Yeditepe University Faculty of Medicine, Department of Emergency Medicine, İstanbul, Turkey
Phone: +90 505 295 36 87 E-mail: mervekoyunoglu@gmail.com ORCID ID: orcid.org/0000-0003-0108-9855

Received/Geliş Tarihi: 10.03.2020 Accepted/Kabul Tarihi: 13.05.2020

©Copyright 2020 Ankara University Faculty of Medicine
Journal of Ankara University Faculty of Medicine is published by Galenos Publishing House.
All content are under CC BY-NC-ND license.



faktörü olarak düşünülmesi gerektiğine ve farklı fiziksel özelliklere bireylerde aynı etkiyi sağlamanın önemli olduğu kanaatindeyiz.

Anahtar Kelimeler: Venöz Tromboembolizm, Pnömatik Kompresyon, Femoral Ven, Ultrasonografi

Introduction

Pulmonary embolism and deep venous thrombosis (DVT) of the lower extremity are the most common form of venous thrombo-embolism (VTE). Despite the observation of rapid advances in emergency care and VTE prophylaxis in the last 50 years, VTE has still been closely related with high morbidity and mortality rates (1,2).

The Virchow triad, which is an important theory in the pathogenesis of VTE, suggests that VTE is observed as a result of decelerated blood flow, vascular endothelial injury and hypercoagulability. Most of the patients with venous thromboembolism have at least one of these factors that constitute the Virchow triad (3-5).

Intermittent pneumatic compression (IPC) devices include inflatable sleeves wrapped around the lower extremities and an electric operated air compressor. The sleeves may be inflated at one time or they may be inflated sequentially as first distally, then proximally to compress legs and increase venous flow. The efficacy of IPC is related to increased peak venous systolic flow rate and flow volume and it also stimulates release of intrinsic fibrinolytic factors while reducing stasis (6-9).

The effects of IPC applications on the venous hemodynamics of the lower extremity have been investigated in many studies (10-13). However, compared to the studies investigating the methods of pharmacological prophylaxis, studies on the aforementioned subject are limited and include smaller sample sizes. Its extent and the pressure to be exerted have not been yet standardized in individuals with varying physiological characteristics.

In studies comparing IPC devices to other methods of VTE prevention, the outcomes of effective prophylaxis observed in patients with different body mass index (BMIs) have not been mentioned. With this point of view, we aimed to investigate the efficacy of IPC devices used in VTE prophylaxis on healthy individuals with different BMIs.

Materials and Methods

Study Population

The study was conducted at the Emergency Department of the Ankara University School of Medicine. This was a cross-sectional, prospective study conducted from November 2014 to May 2015. Written informed assent and consent was obtained

from all participants. Approval for this study was granted by a Local Ethics Committee (date: 27.10.2014, decision no: 17-741-14). Ninety-six limbs in 48 healthy volunteers, without history of Diabetes Mellitus, arterial hypertension, cardiac failure, previous VTE and peripheral arterial disease were recruited for the study. Chronic Venous Failure Classification was used for volunteers with venous failure, and those with varicose veins larger than 3 mm (C2), edema around the feet (C3), venous disease-related pigmentation, stasis dermatitis, dermatosclerosis, white atrophy (C4a, b) or healed ulcers (C5) were excluded from the study (14). The other exclusion criteria was used of antithrombotic or anticoagulant medication and contraceptive treatment.

Study Design

Venous examination was performed by the investigator of the study using the LOGIQ Book XP (General Electric, Logiq XP) and linear probe (8 Mhz) proper for vascular examination, including properties of grey-scaled, colored, spectral, power Doppler ultrasonography (DUS). Prior to IPC device application, the participants were laid in the supine position with their bodies at 10o up; both vena femoralis communis (VFCs) were investigated using longitudinal and transverse sections in grey-scaled ultrasonography. The vein diameters, wall structures, inner surfaces, intraluminal echogenicities, wall irregularities and their qualities were defined. Venous flow patterns were examined comparatively between two extremities and investigated with regard to respiratory phasicity, cardiovascular pulsatility and symmetry using colored DUS. Meanwhile, the arterial blood pressure, heart rate, respiratory rate and oxygen saturation were also measured and recorded. The VFC diameter and venous flow dynamics were evaluated 1-1.5 cm proximal to the junction of VFC and great saphenous vein. The VFC diameter was measured in B-mode imaging and in the transverse plain, between the intimal luminal surfaces. The flow rate of VFC was examined in the longitudinal plain and Doppler spectra. Doppler examination was performed as the Doppler angle did not exceed 60°. The peak systolic rate and diameter of VFC were measured 3 times at 1-minute intervals. The highest measurement was defined as the peak VFC systolic flow. The cross sectional area of VFC was calculated using the formula: $[\pi \times \text{Diameter}^2 / 4]$. Measurements for the right and left VFCs were made separately.

Endpoints

The primary endpoints of this study were (a) measurement of femoral peak systolic velocity and (b) to compare the effects of sequential compression devices in healthy volunteers with different BMIs.

Statistical Analysis

In a one-way ANOVA study, sample sizes of 24, 14, and 10 are obtained from the three groups whose means are to be compared. The total sample of 48 subjects achieves 89% power to detect differences among the means versus the alternative of equal means using an F test with a 0.05000 significance level. The size of the variation in the means is represented by their standard deviation which is 0.08. The common standard deviation within a group is assumed to be 0.15.

The compliance of the measurable continuous variables to the normal distribution was tested using the Shapiro-Wilk test, and the homogeneity of the group variances was examined using the Levene test. The One-way variance analysis was used for the inter-group comparisons between the continuous variables that were compliant with the normal distribution when the number of groups was three or more, and the Kruskal-Wallis variance analysis was used in case the normal distribution was not provided. The Dunnett T3 test was used in the One-way variance analysis in order to investigate the group differing from the others when a difference was observed between the groups, and the multiple comparison test was used in the Kruskal-Wallis variance analysis. In the case where a normal distribution was not provided, the difference between the dependent groups was investigated using the Wilcoxon test in paired samples. The Spearman's correlation coefficient was used to investigate the direction and power of the relation between the non-normally distributed continuous variables and/or sequential variables. A p value lower than 0.05 was accepted as statistically significant.

Results

Study Volunteers Characteristics

The study population included 48 volunteers (26 males, 22 females) with an overall mean age of 28.4 ± 4.8 (median: 28, range: 23-46). The mean height among the participants was 1.68 ± 0.09 m (1.53-1.92), and the mean weight was 73 ± 19 (41-112) kg. The participants were classified into three groups as BMI < 24.9 kg/m² (group I), $25-29.9$ kg/m² (group II), and > 30 kg/m² (group III). Number of cases in group I, II and III were 24 (50%), 14 (29%) and 10 (21%), respectively.

Hemodynamic Changes in Study Volunteers

The mean pulse prior to IPC application decreased from 82 ± 11 /min. (56-110) to 79.5 ± 11 /min. (61-104) after 30 minutes of the procedure (Table 1). The mean pulse measured at the 30th minute of application was significantly decreased compared to that measured prior to the application ($p=0.004$) (Table 1). No significant difference was observed between pre- and post-application measurements of systolic blood pressure, diastolic blood pressure, finger-tip oxygen saturation, or calf and femoral circumferences ($p=N.S.$).

Venous Examination Findings

Venous USG investigations revealed peak venous flow rates of 23.55 ± 4.29 (15.6-34.38) cm/sec, and 22.1 ± 4.17 (14.8-34.38) cm/sec in the right and the left VFCs, respectively. The peak venous flow rate of the right VFC was found to be significantly higher compared to that of left VFC in the resting position ($p<0.001$) (Table 2).

The mean VFC diameter was found to be 0.91 ± 0.13 (0.66-1.13) cm on the right and 0.92 ± 0.12 (0.66-1.15) on the left. The calculated mean cross-sectional area of VFC was 0.66 ± 0.19 (0.34-1) cm² on the right and 0.69 ± 0.18 (0.34-1.04) cm² on the left. The diameter and cross-sectional area of VFC during rest was statistically greater in the left VFC than the right VFC ($p<0.001$) (Table 2).

A statistically significant increase was observed in the mean peak VFC flow rate from 26.17 ± 3.4 cm/sec to 34.49 ± 4.4 cm/sec [mean= $32 \pm 13\%$ (8-55)] on the right, and from 24.66 ± 3.4 cm/sec to 32.37 ± 4 cm/sec [mean= $32 \pm 13\%$ (7-53)] on the left in group I following IPC application ($p<0.05$) (Table 3). In group II, a statistically significant increase was observed in the mean peak VFC flow rate from 22.33 ± 3.38 cm/sec to 28.53 ± 5.3 cm/sec [mean= $27 \pm 13\%$ (12-49)] on the right, and from 20.7 ± 3.4 cm/sec to 26.47 ± 5.15 cm/sec [mean= $28 \pm 17\%$ (5-61)] on the left, as well ($p<0.05$) (Table 3). Finally, in group III, a significant increase was observed in the mean peak VFC flow rate from 18.97 ± 2.3 cm/sec to 21.83 ± 2.55 cm/sec [mean= $15 \pm 4\%$ (9-22)]

Table 1: Comparison of pulse, systolic and diastolic blood pressures and the oxygen saturation measurements before and after IPC application

	IPCb	IPCa
Pulse (/min)	82.14	79.5*
Systolic BP (mmHg)	121.7	123.1
Diastolic BP (mmHg)	77.2	77.02
SatO ₂	97.3	97.5

IPCb: Before intermittent pneumatic compression, IPCa: After intermittent pneumatic compression, BP: Blood pressure

*The mean pulse measured after IPC application was significantly decreased ($p=0.004$)

Table 2: Comparison of diameters, cross-sectional areas and peak flow rates in the right and left VFCs

	Right VFCs	Left VFC
IPCb diameter (cm)	0.91	0.93**
IPCb cross-sectional area (cm ²)	0.66	0.69**
IPCb peak flow rate (cm/sec)	23.55*	22.10

IPCb: Before intermittent pneumatic compression, VFC: Vena femoralis communis

*($p<0.001$) peak venous flow rate of right VFC is significantly higher compared to left VFC.

**($p<0.001$) Diameter and cross-sectional area of VFC; significantly greater in left VFC compared to right VFC

on the right, and from 17.87 ± 1.9 cm/sec to 20.54 ± 1.9 cm/sec [mean= $15 \pm 3\%$ (9-19)] on the left (Table 3).

Comparison of the Effect of Body Mass Index on the Venous Hemodynamics

In the groups classified according to the BMIs of the participants, the effect of IPC on venous hemodynamics was compared; accordingly, a significant difference was observed in the change rates of the diameter, cross-sectional area and peak systolic flow rate of the right VFC ($p=0.006$, $p=0.011$, and $p=0.003$, respectively) (Table 3). Likewise, the effect of IPC on the venous hemodynamics was compared between the three groups, and a significant difference was observed in the change rates of the diameter and peak systolic flow rate of left VFC calculated using the Kruskal-Wallis variance analysis ($p=0.027$, and $p=0.005$, respectively) (Table 3).

The increases observed in the peak systolic flow rates of both right and left VFCs in groups I and II were found to be significantly higher compared to those observed in Group III at the 30th minute of IPC application ($p<0.001$, $p=0.012$, and $p=0.049$, respectively) (Table 3).

Discussion

We compared the effect of IPC on the venous hemodynamics of individuals with different BMIs. Since BMI correlated with the total fat content of overweight and obese individuals, we classified the participants who were healthy volunteers into three groups according to their BMIs. As stated in the methods section, we could classify the participants into three groups according to their BMIs owing to limited by the small number of volunteers for statistically significant results.

In our study, a maximum of 45 mmHg pressure was formed in the calf and femoral regions of the participants. Higher pressures have been used in studies using foot compression devices, and the reported peak venous flow rates have been controversial. In the study of Andrews et al. (15) investigating the effect of foot compression devices on venous flow rate and

volume of healthy individuals, it was reported that the peak flow rates of the femoral vein and popliteal vein were increased by 200-300% with foot compression, and it was possible to obtain a further increase in the peak flow rate by selecting higher pressures and lower frequencies. The effects of foot exercise and IPC on the femoral venous flow were compared in a study conducted in the general intensive care unit of a university hospital, and it was reported that the femoral venous peak flow rate was increased by 10-20% with IPC application to the foot, which was also provided by foot exercises (16). The differences observed in the rates of increases in the peak flow rate in different studies were related to different BMIs of the participants, use of different compression devices and different patient populations in these studies. In a study investigating the femoral venous flow changes in laparoscopic and open gastric by-pass surgeries of obese individuals via USG, the IPC devices were reported to increase the femoral venous flow which decreased during surgery, but were unable to elevate it to basal levels, and therefore it was concluded that IPC should be used in combination with other antithrombotic precautions in these patients (17). Calf and femoral circumference measurements, which are greater in the obese individuals, affected the increase in femoral venous flow rate. In our study, we demonstrated that the same rates of increase could not be statistically provided in individuals with different BMIs. Due to the increased risk of VTE in obese individuals, we believe that the efficacy of the mechanical thrombo prophylaxis method preferred should have been similar to or greater than those of non-obese individuals.

It is true that venous hemodynamics indicated mainly by peak venous velocity or venous volume flow is commonly accepted as a surrogate measure of clinical efficacy of IPC (6). In an effectiveness study comparing 5 IPC devices that were used in 1350 patients, the highest DVT incidence was observed not in the device group showing the least increase in peak velocity but in that showing the greatest increase (18). In a study comparing different types of pneumatic compression devices, no significant difference was observed in the DVT incidence according to the compression methods of the devices

Table 3: Changes in the diameter and flow rates of the right and left vena femoralis communis in groups classified according to the body mass indexes of the participants

IPCb	VFC diameter (cm)	VFC diameter (cm)		IPCb	VFC peak flow rate (cm/sec)		
		IPCa	Change rate (%)		IPCa	Change rate (%)	
Group I (BMI ≤ 24.99)	Right VFC	0.81	0.86	6	26.17	34.49	32
	Left VFC	0.83	0.89	7	24.66	32.37	32
Group II (25-29.99)	Right VFC	0.98	1.0	2	22.33	28.53	27
	Left VFC	1.0	1.04	3	20.72	26.47	28
Group III (BMI ≥ 30)	Right VFC	1.03	1.08	3	18.97	21.83	15*
	Left VFC	1.03	1.08	5	17.87	20.54	15*

IPCb: Before intermittent pneumatic compression, IPCa: After intermittent pneumatic compression, VFC: Vena femoralis communis, BMI: Body mass index

(*): The increases observed in the peak flow rates of both right and left VFCs in group III was found to be significantly lower compared to those observed in group I and II.

and the regions of compression (19). In intermittent pneumatic compression devices, the duration of compression varies to an important extent between the manufacturers (20). Typically, in the compression devices used in DVT prophylaxis, the duration of compression is short and the duration of decompression is 40 seconds or more in order to enable venous filling (21). The intermittent pneumatic compression devices used in our study provided 11 seconds of compression with a 45 mmHg peak pressure, and then 60 seconds of decompression.

Studies on healthy volunteers have demonstrated that IPC devices affected the hemodynamic parameters. In our study, we detected a significant change in the mean pulse of healthy volunteers with IPC application. In the study of Bickel et al. (22), echocardiographic examinations were performed on 20 healthy normotensive individuals, and it was reported that IPC increased the venous return while reducing the systemic vascular resistance, and as a result, increased the cardiac stroke volume without changing the heart rate. We did not use echocardiography, although it is pivotal to have a better understanding of the hemodynamic situation of each participant before, during, and after IPC treatment. In another study including 11 healthy volunteers, the thoracic bio-impedance method was used, and it was demonstrated that IPC devices reduced the cardiac output and the heart rate without causing an increase in cardiac stroke volume (23). The rate of error is high in cardiac output outcomes determined by the bio-impedance method, which is a non-invasive method performed by exposing the thorax to radiofrequency waves (24). We attributed these outcomes observed in these studies evaluating the hemodynamic effects of IPC in healthy volunteers to the different cardiac output measuring methods used. In the study of Bickel et al. (25) investigating the hemodynamic efficacy and safety of IPC application in patients with congestive cardiac failure, IPC was observed to increase the cardiac output (from 4.26 L/min to 4.83 L/min; $p=0.008$) and the stroke volume (from 56.1 mL to 63.5 mL; $p=0.029$) without affecting the heart rate. In order to clearly define the systemic effects of IPC, further studies should be conducted in unstable patient groups with cardiac output measuring methods. We attributed the increase observed in the femoral vein diameter during IPC application to the increased blood flow during the procedure. In a study investigating the effect of IPC on nitric oxide synthesis in the skeletal muscles of rats, an increase in the diameter of the arterioles and veins was observed, as well as in the microcirculation of the cremaster muscle (26). This increase was related to the vasodilatation and reduced systemic vascular resistance observed as a result of nitric oxide release from vascular endothelium secondary to the increased blood flow provided by IPC application. In studies testing nitric oxide inhibitors, this effect of IPC was shown to be blocked and thereby, the mechanism of action of IPC was confirmed (27).

Conclusion

We obtained two main results from this study; that peak blood flow velocity of VFCs measured at the 30th minute of IPC application increased significantly in all groups; group I and II showed a larger increase in peak blood velocity than did group III. We demonstrated that intermittent pneumatic compression application increased the femoral venous flow and this effect could prevent venous stasis; however, this effect changed between individuals with different BMIs, and that the same increase in the femoral vein flow rate could not be obtained between individuals.

Ethics

Ethics Committee Approval: Approval for this study was granted by the Ethical Committee of Ankara University School of Medicine, dated: 27.10.2014, number: 17-741-14.

Informed Consent: Informed written consent was obtained from all the participants.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: M.E., A.B.O., B.G., Ö.A.Ç, Concept: M.E., A.D., M.G.E., Design: M.E., A.D., M.G.E., Data Collection or Processing: M.E., A.B.O., B.G., Ö.A.C., Analysis or Interpretation: M.E., A.D., M.G.E., Literature Search: M.E., A.B.O., B.G., Writing: M.E., A.D., A.B.O.

Conflict of Interest: The authors declare that there are no conflicts of interest regarding the publication of this article.

Financial Disclosure: The authors declared that this study received no financial support.

References

1. Andersson T, Soderberg S. Incidence of acute pulmonary embolism, related comorbidities and survival; analysis of a Swedish national cohort. *BMC Cardiovasc Disord.* 2017;17:155.
2. Guyatt GH, Norris SL, Schulman S, et al. Methodology for the development of antithrombotic therapy and prevention of thrombosis guidelines: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. *Chest.* 2012;141:53S-70S.
3. Coleman DM, Obi A, Henke PK. Update in venous thromboembolism pathophysiology, diagnosis, and treatment for surgical patients. *Curr Probl Surg.* 2015;52:233-259.
4. Virchow RLK. *Gesammelte Abhandlungen zur wissenschaftlichen Medicin.* Frankfurt: Meidinger; 1862.
5. Wolberg AS, Aleman MM, Leiderman K, et al. Procoagulant activity in hemostasis and thrombosis: Virchow's triad revisited. *Anesth Analg.* 2012;114:275-285.
6. Labropoulos N, Cunningham J, Kang SS, et al. Optimising the performance of intermittent pneumatic compression devices. *Eur J Vasc Endovasc Surg.* 2000;19:593-597.
7. Malone MD, Cisek PL, Comerota AJ, et al. High-pressure, rapid-inflation pneumatic compression improves venous hemodynamics in healthy

- volunteers and patients who are post-thrombotic. *J Vasc Surg.* 1999;29:593-539.
8. Kohro S, Yamakage M, Sato K, et al. Intermittent pneumatic foot compression can activate blood fibrinolysis without changes in blood coagulability and platelet activation. *Acta Anaesthesiol Scand.* 2005;49:660-664.
 9. Sutkowska E, Wozniowski M, Gamian A, et al. Intermittent pneumatic compression in stable claudicants: effect on hemostasis and endothelial function. *Int Angiol.* 2009;28:373-379.
 10. Effect of intermittent pneumatic compression on disability, living circumstances, quality of life, and hospital costs after stroke: secondary analyses from CLOTS 3, a randomised trial. *Lancet Neurol.* 2014;13:1186-1192.
 11. Chibbaro S, Cebula H, Todeschi J, et al. Evolution of Prophylaxis Protocols for Venous Thromboembolism in Neurosurgery: Results from a Prospective Comparative Study on Low-Molecular-Weight Heparin, Elastic Stockings, and Intermittent Pneumatic Compression Devices. *World Neurosurg.* 2018;109:e510-e516.
 12. Dennis M, Sandercock P, Graham C, et al. The Clots in Legs Or sTockings after Stroke (CLOTS) 3 trial: a randomised controlled trial to determine whether or not intermittent pneumatic compression reduces the risk of post-stroke deep vein thrombosis and to estimate its cost-effectiveness. *Health Technol Assess.* 2015;19:1-90.
 13. Kakkos SK, Caprini JA, Geroulakos G, et al. Combined intermittent pneumatic leg compression and pharmacological prophylaxis for prevention of venous thromboembolism in high-risk patients. *Cochrane Database Syst Rev.* 2008; CD005258.
 14. Classification and grading of chronic venous disease in the lower limbs. A consensus statement. Ad Hoc Committee, American Venous Forum. *J Cardiovasc Surg (Torino)* 1997;38:437-441.
 15. Andrews B, Sommerville K, Austin S, et al. Effect of Foot Compression on the Velocity and Volume of Blood-Flow in the Deep Veins. *British Journal of Surgery.* 1993;80:198-200.
 16. Yamashita K, Yokoyama T, Kitaoka N, et al. Blood flow velocity of the femoral vein with foot exercise compared to pneumatic foot compression. *J Clin Anesth.* 2005;17:102-105.
 17. Nguyen NT, Cronan M, Braley S, et al. Duplex ultrasound assessment of femoral venous flow during laparoscopic and open gastric bypass. *Surgical Endoscopy and Other Interventional Techniques.* 2003;17:285-290.
 18. Proctor MC, Greenfield LJ, Wakefield TW, et al. A clinical comparison of pneumatic compression devices: the basis for selection. *J Vasc Surg.* 2001;34:459-463.
 19. Koo KH, Choi JS, Ahn JH, et al. Comparison of clinical and physiological efficacies of different intermittent sequential pneumatic compression devices in preventing deep vein thrombosis: a prospective randomized study. *Clin Orthop Surg.* 2014;6:468-475.
 20. Morris RJ. Intermittent pneumatic compression - systems and applications. *J Med Eng Technol.* 2008;32:179-188.
 21. Morris RJ, Griffiths H, Woodcock JP. Analysis of the operation of the SCD Response intermittent compression system. *J Med Eng Technol.* 2002;26:111-116.
 22. Bickel A, Shturman A, Grevtzev I, et al. The physiological impact of intermittent sequential pneumatic compression (ISPC) leg sleeves on cardiac activity. *Am J Surg.* 2011;202:16-22.
 23. Fanelli G, Zasa M, Baciarello M, et al. Systemic hemodynamic effects of sequential pneumatic compression of the lower limbs: a prospective study in healthy volunteers. *J Clin Anesth.* 2008;20:338-342.
 24. Albert NM, Hail MD, Li J, et al. Equivalence of the bioimpedance and thermodilution methods in measuring cardiac output in hospitalized patients with advanced, decompensated chronic heart failure. *Am J Crit Care.* 2004;13:469-479.
 25. Bickel A, Shturman A, Sergeiev M, et al. Hemodynamic effect and safety of intermittent sequential pneumatic compression leg sleeves in patients with congestive heart failure. *J Card Fail.* 2014;20:739-746.
 26. Chen LE, Liu K, Qi WN, et al. Role of nitric oxide in vasodilation in upstream muscle during intermittent pneumatic compression. *J Appl Physiol (1985).* 2002;92:559-566.
 27. Liu K, Chen LE, Seaber AV, et al. Intermittent pneumatic compression of legs increases microcirculation in distant skeletal muscle. *J Orthop Res.* 1999;17:88-95.