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Medical Compression Stockings Significantly Increase Local Tissue Factor Levels in Advanced Chronic Venous Insufficiency Patients and Healthy Volunteers

Christopher R. Lattimer,[1,2] Evi Kalodiki,[1,2] Patrick Van Dreden,[3] Aurelie Rousseau,[3] Grigorios T. Gerotziafas[4,5]. [1]Vascular Surgery, Josef Pflug Vascular Laboratory, Ealing Hospital, and Imperial College; [2]West London Vascular and Interventional Centre; [3]Clinical Research Department, Stago; [4]Haematology, Hopitaux Universitaires de l'Est Parisien-APHP; [5]Cancer Biology and Therapeutics, Centre de Recherche Saint-Antoine, Sorbonne Universite

Objective: Evidence that medical compression stockings (MCS) prevent deep venous thrombosis (DVT) is weak. Furthermore, the body position that predisposes to DVT is not fully known. It is assumed that standing is protective through involuntary leg muscle contractions and that lying stationary may provoke DVT. Previous work using ultrasound has shown the presence of venous sludge in the popliteal veins, in both positions. The aim was to investigate the effect of standing, lying, and compression on thrombogenicity. This was achieved by taking local venous blood samples and measuring an array of factors considered relevant in thrombogenesis.

Methods: Patients with advanced chronic venous insufficiency awaiting endothermal ablation (C4a, C4b) and healthy volunteers (n = 14 legs in each group, 1 leg per patient) had local leg blood samples taken after 1 hour of standing, lying, and standing with compression on separate days. Knee-length MCS of 23 to 32 mm Hg were administered. Platelet-poor plasma samples were analyzed for procoagulant phospholipids, tissue factor, D-dimer, fibrin monomer, and factor VIIa-antithrombin complexes. This was in addition to a thrombin generation test using the PPP-reagent, which measured lag time, endogenous thrombin potential, peak, time to peak, and mean rate index.

Results: The most responsive was tissue factor, with significant increases after an MCS was worn in standing compared with lying and standing with compression in both volunteers and patients (Fig 1). Standing and compression made no difference to D-dimer or factor VIIa-antithrombin levels in either group (Table). Thrombin generation testing revealed no differences in the volunteer group, but in the patients, compression appeared to have a favorable significant effect in four of five measurements compared with lying (Table).

Conclusions: Local tissue factor concentrations were elevated significantly with MCS. This was on a background of unaffected D-dimer and factor VIIa-antithrombin levels, thereby questioning the thrombogenic significance of the elevated tissue factor. However, compression reduced thrombin generation parameters, but only in patients with chronic venous insufficiency. Patients also demonstrated significantly reduced thrombin generation when standing compared with lying. This research supports our hypothesis that standing and compression may offer additional protection from thrombosis, but only in patients.

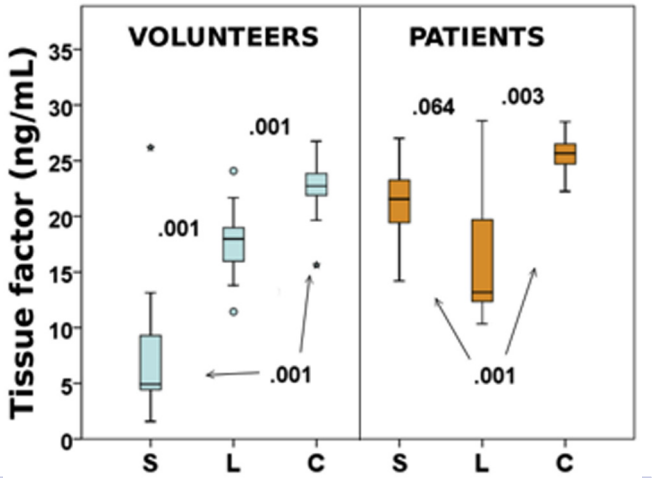

Fig. Local tissue factor concentrations in response to standing (*S*), lying (*L*), and compression (*C*) in volunteers and patients. Significance levels are shown (Wilcoxon).

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Effectiveness of the PowerWire Radiofrequency Guidewire in Recanalizing Chronically Occluded Iliac Venous Stents

Newton Neidert, Haraldur Bjarnason. Mayo Clinic, Rochester, Mimn

Objective: Iliac venous stenting is a commonly performed procedure in treating post-thrombotic and nonthrombotic iliac venous disease. Whereas overall stent patency rates are high, stent occlusion does occur. Recanalizing chronically occluded stents is technically challenging and often impossible with conventional guidewires and catheters. The PowerWire (Baylis Medical, Burlington, Mass) radiofrequency guidewire is a 0.035-inch guidewire that delivers radiofrequency energy at the end of the guidewire.

Methods: A retrospective chart review was conducted of patients with chronically occluded iliac venous stents who underwent an iliac venous recanalization attempt using the PowerWire from March 2015 to June 2018. A total of 15 patients underwent a recanalization attempt with the PowerWire. All patients had initial unsuccessful attempts at recanalizing the occluded iliac vein stents with conventional guidewires.

Table. Median (interquartile range) values in three different laboratory situations for 1 hour

	Volunteers			Patients (C4)		
Parameters	Standing	Lying	Compression	Standing	Lying	Compression
Procoagulant phospholipids, $	**67.7 (63.5-80)**[a]	76.7 (66.6-92.6)	71.5 (67-80.7)	82.8 (74.7-91.2)	89.5 (76.3-96.5)	**77.1 (67.6-81.8)**[a]
Tissue factor, ng/mL	**4.94 (4.03-10)**[a]	17 (15.5-19.1)	**22.7 (21.7-23.9)**[b]	21.6 (18.7-23.3)	13.2 (12.2-20.4)	**25.7 (24.6-26.7)**[b]
D-dimer, µg/mL	0.27 (0.27-0.34)	0.27 (0.27-0.32)	0.27 (0.27-0.45)	0.35 (0.27-0.9)	0.34 (0.28-0.63)	0.29 (0.27-0.53)
Fibrin monomer, µg/mL	5 (5-5.8)	5 (5-60.3)	5 (5-50.4)	5 (5-7.32)	5 (5-5.07)	5 (5-5)
Factor VIIa, units/mL	74.7 (55.2-300)	71.9 (54.3-54.5)	**17.3 (10.6-241)**[a]	26.7 (19.7-55.5)	28.1 (19.9-55.9)	32.5 (24.6-67.5)
Lag time, minutes	6.74 (5.49-8.92)	5.91 (4.74-7.16)	5.67 (4.67-6.93)	6.75 (5.04-9.13)	6.46 (5.06-7.42)	7.25 (5.33-8.88)
ETP, µM/min	1.1 (0.75-1.25)	1.1 (0.72-1.72)	1 (0.77-1.54)	0.94 (0.84-1.08)	1.08 (0.68-1.38)	0.96 (0.43-1.11)[a]
Peak, nM	150 (95.5-194)	1.69 (95.2-349)	136 (97.3-291)	150 (101-182)	**175 (108-214)**[a]	**150 (62.8-185)**[a]
ttPeak, minutes	10.8 (9-12.3)	8.83 (7.87-11.2)	9.83 (7.55-10.8)	10.8 (8.51-13.7)	**10 (7.9-11.9)**[a]	**10.9 (8.67-12.9)**[a]
MRI	40.8 (21.7-61.1)	48.6 (24.3-150)	36.7 (24.1-107)	44.9 (21.3-56.6)	**51.3 (31.3-69.4)**[a]	**41.9 (18.8-56.7)**[a]
Factor VIIa-antithrombin, ρM	102 (82.5-179)	115 (57.4-227)	82.9 (53.6-194)	118 (91.4-161)	111 (97-133)	118 (101-146]

ETP, Endogenous thrombin potential; *MRI,* mean rate index; *ttPeak,* time to peak.
[a]$P < .05$ vs standing.
[b]$P < .05$ vs lying.

Successful recanalization was defined as restoration of antegrade iliac venous flow after angioplasty alone or angioplasty and placement of additional stents.

Results: Percutaneous recanalization of chronically occluded iliac venous stents using the PowerWire was successful in 10 patients. Cumulative 6-month patency rate was 62%. Cumulative 12-month patency rate was 43%. There were two complications that occurred with use of the PowerWire. One patient had transient footdrop of the ipsilateral limb that was successfully recanalized. One patient had self-limited perforation of the left common iliac artery during unsuccessful recanalization.

Conclusions: The PowerWire is an effective and relatively safe device for recanalizing chronically occluded iliac venous stents.

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Impact of Presence of Inferior Vena Cava Filter on Iliocaval Stent Outcomes

Arjun Jayaraj, Laura Lamanilao, Seshadri Raju. RANE Center for Venous and Lymphatic Disease at St. Dominic Hospital

Objective: The impact of presence of an inferior vena cava (IVC) filter in patients undergoing stenting for symptomatic femoroiliocaval obstruction has not been explored in detail. This study attempted to fill this gap by evaluating clinical and stent-related outcomes in such patients. The incidence of deep venous thrombosis (DVT) in this setting was also analyzed.

Methods: A retrospective review of contemporaneously entered electronic medical record data on initial iliocaval stents placed in patients with an indwelling IVC filter (or placed after stenting) during a 15-year period from 2000 to 2015 was performed. A separate cohort that underwent initial stenting during the time frame but that did not have an IVC filter was used as the control group. Clinical outcomes were evaluated through use of the Venous Clinical Severity Score (VCSS). The incidence of DVT was reviewed in both groups. Kaplan-Meier analysis was used to assess stent patency after intervention, whereas paired *t*-test was used to examine preintervention and postintervention outcomes within and between groups.

Results: A total of 57 patients underwent placement of a femoroiliocaval stent in the setting of a pre-existing (46) or post-stent (11) IVC filter (filter group). The control group had 359 patients. There was no difference in VCSS at baseline between the two groups. During a median follow-up of 59 months, VCSS went from 5 to 2 at 12 months ($P = .84$) in the filter group and from 5 to 3.5 in the control group ($P < .01$). However, there was no statistically significant difference in the VCSS between the two groups at 12 months ($P = .09$). The incidence of ipsilateral DVT in the filter group was 7%, and that in the treatment group was 3% ($P = .10$). There were no contralateral DVTs in either group. Median primary, primary assisted, and secondary patencies in the filter/control groups were 116/64 ($P < .01$), 137/58 ($P < .01$), and 29/30 months ($P = .77$).

Conclusions: Presence of an IVC filter does not appear to affect clinical outcomes after femoroiliocaval stenting. However, counterintuitively, they appear to confer better primary and primary assisted stent patencies.

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Improvement in Quality of Life After Iliac Vein Stenting in a Prospective Clinical Study of a Nitinol Venous Stent

William Marston,[1] Mahmood Razavi[2]. [1]University of North Carolina School of Medicine; [2]St. Joseph's Hospital, Orange, Calif

Objective: Stenting of the iliofemoral venous outflow tract is recommended to treat patients with significant limb symptoms related to obstruction. However, it remains unclear which patients benefit most from iliac vein stenting. In this prospective clinical trial studying the performance of a nitinol stent designed for the treatment of venous obstructive disease, quality of life (QOL) measures were related to patient and procedural characteristics to determine which patients benefit most from venous stenting.

Methods: There were 170 patients with chronic iliofemoral venous obstruction enrolled in a prospective pivotal trial studying the effectiveness of a nitinol venous stent (Veniti, Inc, Fremont, Calif). Before intervention, QOL was measured with the Venous Clinical Severity Score (VCSS) and Chronic Venous Insufficiency Questionnaire (CIVIQ-2) score. Venography was performed, and the presence of vessel stenosis of >50% was required for study inclusion. Intravascular ultrasound (IVUS) was also performed before and after stent insertion to allow calculation of lumen diameter and area. QOL was measured with VCSS and CIVIQ-2 at 1 month, 6 months, and 12 months after stenting, and repeated venography and IVUS were performed at 12 months.

Results: Of the cohort, 140 had QOL measures performed before stenting and at 12 months of follow-up. Of these, 133 had IVUS measurements at the time of stent insertion and 94 had IVUS at 12 months. Both VCSS and CIVIQ-2 score improved significantly at 1 month and 12 months after stenting as noted in the Table. Improvement in VCSS was similar in patients treated for nonthrombotic (5.2 ± 5.6 points) and post-thrombotic (4.0 ± 3.9 points) disease. Patients who experienced significant improvement in VCSS (≥3 points; n = 91) had a significantly higher mean maximal area stenosis on IVUS before stenting (70.1% ± 20%) than 32 patients who had <2 points of improvement on VCSS (57.2% ± 25.9%; $P = .007$). VCSS improvement at 12 months did not correlate with the maximal percentage diameter or percentage area stenosis on IVUS at 12 months.

Conclusions: The majority of patients treated with venous stenting for symptomatic iliofemoral venous obstruction experience significant reduction in symptoms that is durable to 12 months of follow-up. QOL improvement was significantly more frequent in patients stented for more severe venous obstruction.

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Relevance of Thrombophilia Testing in Patients Undergoing Iliofemoral Venous Stenting for Post-Thrombotic Occlusion

Laura Tincknell,[1] Adam Gwozdz,[1] Nicholas Jackson,[1] Justinas Silickas,[1] Alberto Smith,[1] Prakash Saha,[1] Karen Breen,[2] Stephen Black[1]. [1]Academic Department of Vascular Surgery, School of Cardiovascular Medicine and Science, St Thomas' Hospital, King's College London; [2]Department of Haematology, St Thomas' Hospital, King's College London

Objective: Inherited and acquired thrombophilias increase the risk of venous thromboembolism (VTE), and the antiphospholipid antibody syndrome (APS), an acquired thrombophilia, is associated with a high risk of recurrent VTE. Postoperative anticoagulation therapies remain tailored, with APS patients requiring long-term vitamin K antagonists (VKAs) compared with direct oral anticoagulants for patients with inherited thrombophilia. As such, iliofemoral venous stenting in patients with thrombophilia is controversial. The aim of this study was to examine the association of thrombophilia with cumulative patency and reintervention rates after stenting for post-thrombotic occlusion.

Methods: Consecutive patients (2012-2017) receiving a nitinol venous stent for post-thrombotic disease with a minimum of 1-year follow-up were included for analysis. Thrombophilia testing was performed when VTE occurred at a young age with weak provoking factors, strong family history, or recurrence. Patients with strong risk factors for VTE were not tested and were excluded from analysis. All patients were given therapeutic dose low-molecular-weight heparin divided twice daily for 2 weeks after the procedure, followed by a VKA for 6 months. Patients with APS continued on long-term VKA therapy at 6 months, whereas all other patients were transitioned to direct oral anticoagulants. Stent

Table. Venous Clinical Severity Score (*VCSS*) and Chronic Venous Insufficiency Questionnaire (*CIVIQ-2*) score at 1 month and 12 months

	Before stenting	1 month after stenting	12 months after stenting	*P* value before vs 1 month	*P* value before vs 12 months
VCSS	9.9 ± 5.0	6.3 ± 4.3	5.7 ± 4.3	<.00001	<.000001
CIVIQ-2	0.44 ± 0.24	0.30 ± 0.25	0.27 ± 0.25	<.00001	<.00001