Effect of iliofemoral-caval venous intervention on lower extremity compartment pressure in patients with chronic venous insufficiency

Taimur Saleem, MBBS, Alexander Knight, BS, *and* Seshadri Raju, MD, FACS, *Jackson, Miss*

ABSTRACT

Background: Chronic compartment syndrome (CCS) secondary to venous hypertension from chronic venous insufficiency is an uncommonly described entity. The measurement of high resting compartment pressure is helpful in establishing the diagnosis of CCS. The effect of deep venous intervention on compartment pressures in patients with chronic venous insufficiency is not well described. This study evaluated a subset of patients with signs and symptoms of venous disease in whom intervention (hyperdilation or new endovenous stent placement) was performed on the iliofemoral-caval venous system. The effect of the specific intervention was objectively measured by documenting preoperative and postoperative compartment pressures in the posterior superficial compartment of the calf at rest in the supine position.

Methods: From January 2018 to January 2019, there were 80 limbs that underwent either hyperdilation (n = 34) or new endovenous stent placement (n = 46). All patients had measurement of compartment pressures before and after intervention with a simple needle manometer system. Values of 15 mm Hg or higher were considered indicative of CCS in the appropriate clinical context. Clinical parameters such as pain, swelling, and Venous Clinical Severity Score were measured preoperatively and postoperatively.

Results: Venous intervention in the form of hyperdilation or endovenous stent placement was associated with reduction in compartment pressure of the extremity undergoing the intervention. In the new stent subset, the compartment pressure was reduced from 17.4 (±4.9) mm Hg to 12.6 (±3.7) mm Hg ($P < .0001$). In the hyperdilation subset, the compartment pressure was reduced from 14.9 (±4.1) mm Hg to 10.3 (±2.7) mm Hg ($P < .0001$). There was also a significant improvement in pain, swelling, and Venous Clinical Severity Score after intervention. In patients undergoing hyperdilation, there was a significant improvement in the ejection fraction of the calf pump after intervention from 54.8% (±23.1%) to 52.1% (±18.7%; $P = .009$).

Conclusions: Deep venous intervention in the form of hyperdilation or endovenous stent placement was associated with symptomatic improvement and reduction of compartment pressure of the extremity undergoing intervention. (J Vasc Surg: Venous and Lym Dis 2020;8:769-74.)

Keywords: IVUS; Intravascular ultrasound; Iliac vein stent; Hyperdilation; Compartment pressure; Chronic compartment syndrome

Compartment syndrome is the result of increased tissue pressure within a restricted myofascial space. If left untreated, it can result in irreversible ischemia of vital neuromuscular structures.[1] Compartment syndrome can occur in patients with venous disease. Acute compartment syndrome manifested as phlegmasia cerulea dolens has been described in association with extensive lower extremity acute deep venous thrombosis. Chronic compartment syndrome (CCS) secondary to venous hypertension from chronic venous insufficiency is an uncommonly described entity in the literature.[2] This condition can also be a source of claudication in patients who have other signs and symptoms of venous disease. CCS can also be seen in patients with blunt trauma or tumors and with overuse in athletes such as runners.[3]

The measurement of compartment pressure is helpful in establishing the diagnosis of CCS. However, the threshold for compartment pressure used to define CCS is not well defined. It is also not known whether chronic venous compartment syndrome affects all leg compartments uniformly. Normal compartment pressure has been reported to be <15 mm Hg. In a previous publication, compartment pressure >15 mm Hg in the posterior superficial calf compartment has been noted to support the diagnosis of CCS secondary to venous hypertension.[3,4] Because of the chronic nature of the

From The RANE Center for Venous and Lymphatic Diseases, St Dominic's Memorial Hospital.

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Correspondence: Taimur Saleem, MBBS, The Rane Center, St Dominic's Memorial Hospital, 971 Lakeland Dr, Ste 401, Jackson, MS 39216 (e-mail: taimur@gmail.com).

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condition in CCS, pathologic compartment pressure would be lower than that seen in patients with acute compartment syndrome or phlegmasia cerulea dolens (35-40 mm Hg) or in patients with ischemic reperfusion injury after arterial revascularization (25-30 mm Hg).

The aim of this report was to evaluate a subset of patients with signs and symptoms of venous disease in whom intervention (hyperdilation or new endovenous stent placement) was performed on the iliofemoral-caval venous system. The effect of the specific intervention was objectively measured by documenting preoperative and postoperative compartment pressures in the calf in the posterior superficial compartment of the extremity undergoing the intervention at rest in the supine position.

METHODS

Type of research study. From January 2018 to January 2019, records of all patients who had either hyperdilation or new stent placement along with measurement of resting compartment pressures were analyzed for this study. All these patients had measurement of compartment pressures before and after intervention in the supine position. This is a single-center study (three surgeons). All data were contemporaneously entered into a time-stamped electronic medical record and analyzed retrospectively. Informed consent was obtained from patients. Institutional Review Board permission was granted for publication of the study.

Inclusion and exclusion criteria. Included participants were patients who had clinical signs and symptoms, clinical history, and preoperative investigative studies suggestive of venous disease and in whom the symptoms were significant enough to interfere with work or daily living or both and were not controlled with conservative measures alone. Patients who received new venous stents had failed to respond to conservative therapy (including measures such as leg elevation, use of graduated compression stockings [30-40 mm Hg], and local wound care) for at least 6 months. The primary indication for reintervention in the form of hyperdilation was significant residual or recurrent symptoms such as pain, swelling, cellulitis, or venous ulceration not responsive to compression therapy and wound care for at least 6 months. On duplex ultrasound, flow channel reduction by at least 50% due to either in-stent restenosis or stent compression was considered significant. However, the decision to reintervene depended on the composite of the patient's symptoms and the duplex ultrasound findings.[5] All patients with nonvenous causes of limb symptoms were excluded from this study. This determination of exclusion was made on the basis of a comprehensive clinical history, detailed physical examination, and noninvasive techniques such as ultrasound.

ARTICLE HIGHLIGHTS

- **Type of Research:** Single-center, retrospective study
- **Key Findings:** Venous interventions in 80 limbs including hyperdilation and endovenous stent placement were associated with reduction in compartment pressure of the extremity. There was also a significant improvement in pain, swelling, and Venous Clinical Severity Score after intervention.
- **Take Home Message:** Deep venous intervention including hyperdilation and endovenous stent placement results in symptomatic improvement and reduction of compartment pressure.

Clinical parameters. Swelling was assessed by physical examination and was graded 0 to 4 (grade 0, none; grade 1, pitting but not obvious; grade 2, ankle edema; grade 3, gross involving the leg; grade 4, gross involving the whole limb). Pain was assessed by the visual analog scale (VAS) score (0-10).[6,7] Venous Clinical Severity Score (VCSS) was also assessed. These clinical parameters were assessed preoperatively, at 6 weeks, and at 3- to 6-month intervals thereafter. Swelling was considered improved if there was an improvement of at least one grade.[6] Pain was considered improved if there was an improvement of at least 2 points by VAS score (2/10).

Preoperative and postoperative evaluation. The duplex ultrasound technique for examinations performed in our clinic and the intravascular ultrasound (IVUS) technique performed in the operating suite for new stent placement or hyperdilation have previously been described in detail.[6,8] Appropriately selected patients underwent a comprehensive preoperative and postoperative evaluation including duplex ultrasound scan, ambulatory venous pressure measurements (percentage drop, venous filling time, and air plethysmography venous filling index).[8]

Procedural technique. Access is typically obtained at the midthigh or lower thigh femoral vein (second-order vein) followed by the placement of an 11F sheath. This is followed by ascending venography and IVUS examination. In patients requiring new stent placement, IVUS was used to delineate the iliocaval confluence and the ideal distal landing zone.[9] The type of stent used was Wallstent (Boston Scientific, Marlborough, Mass) with the addition of Z stent (Cook Medical, Bloomington, Ind) in some cases in which additional radial strength was needed at the iliocaval confluence. Isodilation refers to restoration of a previously placed resident venous stent to its rated diameter. Hyperdilation (also referred to as overdilation in some literature) refers to balloon dilation of a resident venous stent to beyond its rated diameter. Restoration of the rated diameter of the stent is generally

the goal, but this is often not possible to achieve because of complex factors such as stent compression. That is why a higher caliber balloon and the technique of hyperdilation may be required to restore the nominal diameter of the stent.[5] Determination of optimal stent sizes in the common iliac, external iliac, and common femoral vein segments has been made to be diameters of 16 mm (area, 200 mm^2), 14 mm (area, 150 mm^2), and 12 mm (area, 125 mm^2), respectively. These correspond to the minimal sizes needed for optimal flow calculated from flow hemodynamic equations such as Poiseuille's equation and Young's scaling ratios based on IVUS observation of normal iliac vein segments in healthy individuals.[6] In patients requiring hyperdilation, IVUS provides valuable information about stent compression or degree of in-stent restenosis. IVUS also provides important post-intervention data. We have recently shown that hyperdilation rather than isodilation provides more durable caliber improvement, better clinical outcomes, and decrease in venous hypertension.[5] Hyperdilation is performed with target caliber (4- or 6-cm length) Atlas balloons (Bard Inc, Murray Hill, NJ). In our experience, the Wallstent tolerates hyperdilation well up to 4 mm beyond the rated stent diameter without any obvious disruption of structural integrity of the stent.[5]

Compartment pressure measurement. Compartment pressures were measured preoperatively in the operating room before the performance of any venous intervention. The patients were in supine position at rest. Repeated measurement was performed postoperatively after the venous intervention to ascertain the effect of the intervention. The same site was used for measurement of the pressures before and after intervention and was marked. After the preintervention measurement, the needle was removed and then reinserted at the same site after intervention. The apparatus used for compartment pressure measurement was a simple needle manometer system using a 16-gauge needle. Local anesthetic was not used in this study. The posterior superficial compartment in the calf was used for pressure measurement in all patients based on tactile feel. Although it was not used in this study, ultrasound may be used as a guide to needle placement for elective compartment pressure measurement. Based on previous reports, patients with compartment pressure measurement >15 mm Hg in the posterior superficial calf compartment were considered to have CCS.[2]

Anticoagulation protocol. Patients with hyperdilation or new stent placement receive prophylactic low-molecular-weight heparin for 24 to 48 hours starting before the procedure. Bivalirudin 75 mg is also administered during the procedure. Postoperatively, long-term anticoagulation is used in selected patients only.[5]

Stent surveillance. Our stent surveillance protocol has previously been described in detail.[7] Briefly, stent surveillance was performed at postoperative day 1, at 2 weeks, and at 4 weeks initially. Patients were seen in the clinic at 6 weeks, at 3 months, and at 6-month or annual intervals thereafter. Typically, stent surveillance was performed at each of the clinical visits in addition to the first postoperative month.

Statistical analysis. Statistical analysis was performed using a commercially available statistics program (Prism Software, Irvine, Calif). Mean and standard deviations were reported. Where appropriate, two-tailed and unpaired *t*-test was used for analysis. Multivariate logistic regression analysis was also performed. $P < .05$ was considered significant.

RESULTS

Demographics. From January 2018 to January 2019, a total of 2200 patients were seen in our clinic with 836 new patient evaluations; 80 limbs underwent either hyperdilation (n = 34 limbs) or new endovenous stent placement (n = 46 limbs) along with measurement of compartment pressures at the time of the intervention in the supine position. The median age for patients undergoing new endovenous stent placement or hyperdilation was 65 years and 52 years, respectively (Table I); 63% of patients had post-thrombotic syndrome, whereas May-Thurner syndrome was present in 32% of patients. Four limbs (5%) had a mixed etiology (post-thrombotic syndrome and May-Thurner syndrome). Superficial reflux was present in 19 limbs (24%), whereas deep reflux was present in 22 limbs (27%); 10 limbs (12%) had both superficial and deep reflux. Clinical, Etiology, Anatomy, and Pathophysiology (CEAP) distribution of patients was as follows: class 3, 25 (31.3%); class 4, 45 (56.2%); class 5, 8 (10%); and class 6, 2 (2.5%).

Compartment pressure. Intervention was performed in the form of hyperdilation or new stent placement. New stents were placed in patients with signs and symptoms of venous disease in whom conservative measures had failed and in whom IVUS showed a stenosis in the iliofemoral venous system. Optimal stent size in the common iliac, external iliac, and common femoral vein segments was determined to be a diameter of 16 mm (area,

Table I. Demographic details of patients undergoing new stent placement or hyperdilation

Demographic data	New stents (45 patients [46 limbs])	Hyperdilation (29 patients [34 limbs])
Median age, years (range)	65 (24-86)	52 (28-79)
Male:female	1:2	1:5
Right:left	1:1	2:3
Nonthrombotic:post-thrombotic	1:3	1:1

Table II. Compartment pressure before and after intervention

	Before intervention	After intervention	*P* value
New stents (n = 46)	17.4 ± 4.9	12.6 ± 3.7	<.0001[a]
Hyperdilation (n = 34)	14.9 ± 4.1	10.3 ± 2.7	<.0001[a]

Values (in mm Hg) are reported as mean ± standard deviation.
[a] *P* value significant.

200 mm^2), 14 mm (area, 150 mm^2), and 12 mm (area, 125 mm^2), respectively. Adjacent vein was not used as a comparator because Rokitansky-type lesions (diffuse venous lesions involving tandem segments) are present in many patients, and this can lead to undertreatment of venous disease. The areas mentioned correspond to the minimal sizes needed for optimal flow calculated from flow hemodynamic equations such as Poiseuille's equation and Young's scaling ratios based on IVUS observation of normal iliac vein segments in healthy individuals.[6] Hyperdilation was performed in patients with residual or recurrent symptoms not controlled with conservative measures alone and in whom ultrasound suggested stent malfunction in the form of narrow stent diameters due to stent compression or in-stent restenosis.

Intervention in the form of hyperdilation or new endovenous stent placement was associated with a significant reduction in the compartment pressure of the posterior superficial calf compartment (Table II). Mean compartment pressure before intervention was 17.4 mm Hg in the subset undergoing new stent placement and 14.9 mm Hg in the subset undergoing hyperdilation. After intervention, mean compartment pressure was 12.6 mm Hg and 10.3 mm Hg in the new stent and hyperdilation subsets, respectively. In both groups, there was a reduction of compartment pressures after intervention.

Clinical parameters. Deep venous system intervention was also significantly associated with improvement in the VCSS, VAS pain score, and lower extremity swelling for the new stent subset of patients. For hyperdilation patients, intervention was significantly associated with improvement in the VCSS and VAS pain score (Table III).

Table III. Effect of intervention on Venous Clinical Severity Score (*VCSS*), visual analog scale (*VAS*) pain score, and swelling

	Before intervention	After intervention	*P* value
New stent (46 limbs)			
VCSS	5.9 ± 2.7	3.8 ± 2.3	<.0001[a]
VAS pain score	6.2 ± 2.8	3.8 ± 2.9	<.0001[a]
Swelling	2.1 ± 1.1	1.4 ± 1.3	.0005[a]
Hyperdilation (34 limbs)			
VCSS	5.5 ± 3.8	4.1 ± 3.9	.003[a]
VAS pain score	6.6 ± 2.4	5 ± 2.9	.04[a]
Swelling	1.8 ± 1.3	1.6 ± 1.2	.6

Values are reported as mean ± standard deviation.
[a] *P* value significant.

Table IV. Association of body mass index (*BMI*) and compartment pressure at baseline

Subset	BMI <30 kg/m^2	BMI >30 kg/m^2	*P* value
Hyperdilation	13.9 ± 3.9	15.7 ± 4.2	.2
New stents	16.7 ± 6.8	17.6 ± 4.3	.6
Combined subset	15 ± 5.3	16.9 ± 4.3	.1

Values (in mm Hg) are reported as mean ± standard deviation.

Obesity and venous stenosis. Compartment pressure at baseline (before intervention) was not found to be significantly associated with body mass index (Table IV). Degree of stenosis measured by IVUS did not appear to be significantly associated with the reduction in compartment pressure (Table V).

Air plethysmography parameters. In the hyperdilation subset of patients, intervention was significantly associated with a change in the ejection fraction of the calf pump (Table VI). Despite symptomatic improvement in patients, other air plethysmography parameters did not show a significant change on analysis.

Follow-up. There were no perioperative complications noted in our study. Median follow-up was 6 months. Mean follow-up was 4.5 months (±2 months).

Logistic regression analysis. Logistic regression analysis was performed using change in compartment pressure of 5 mm Hg or more and presence of lymphedema as dependent variables. However, none of the associations were significant (Tables VII and VIII).

DISCUSSION

This study showed the effect of deep venous intervention in the form of new endovenous stent placement or hyperdilation on the compartment pressures in the lower extremity. Improvement in clinical parameters such as VCSS, VAS pain score, and swelling was noted with deep venous intervention.

Presence of chronic venous compartment syndrome requires a high index of suspicion based on comprehensive clinical history and detailed physical examination.

Table V. Association of degree of stenosis as measured by intravascular ultrasound (*IVUS*) and reduction in compartment pressure

Subset	IVUS stenosis <50%	IVUS stenosis >50%	*P* value
Hyperdilation	4.6 ± 2.6	4.5 ± 4.7	.8
New stents	4.4 ± 3.8	5.8 ± 4.3	.3
Combined subset	4.5 ± 3.4	3.7 ± 4.7	.5

Values (in mm Hg) are reported as mean ± standard deviation.

Table VI. Air plethysmography parameters in patients undergoing new stent placement or hyperdilation

	Before intervention	After intervention	*P* value
New stents (n = 46)			
VV, mL	62.9 ± 36.5	68.2 ± 33.5	.48
EV, mL	35.4 ± 26.9	39.9 ± 26.4	.5
EF, %	56.1 ± 23.3	55.7 ± 26.6	.3
RT, seconds	15.7 ± 7.4	15.1 ± 6.6	.9
RVF, %	31.8 ± 25.3	33.3 ± 20.9	.9
VFI_{90}	1.3 ± 1.1	1.4 ± 1.1	.3
Hyperdilation (n = 34)			
VV, mL	71.7 ± 38.9	72.5 ± 45.6	.8
EV, mL	41.5 ± 29.2	42.1± 20.4	.1
EF, %	54.8 ± 23.1	52.1 ± 18.7	.009[a]
RT, seconds	15.8 ± 11.4	16.1 ± 9.9	.7
RVF, %	38.1 ± 27.8	38.8 ± 15.2	.06
VFI_{90}	1.8 ± 1.4	2.4 ± 2.5	.2

EF, Ejection fraction; *EV,* ejection volume; *RT,* recovery time; *RVF,* residual volume fraction; *VFI_{90},* venous filling index; *VV,* venous volume. Values are reported as mean ± standard deviation.
[a] *P* value significant.

Measurement of compartment pressures supports the diagnosis of chronic venous compartment syndrome. In patients with CCS due to venous insufficiency, an initial limited trial of conservative measures may be considered. However, intervention should be considered early in the course of the disease process and especially when conservative measures fail or there is development of associated neurologic symptoms, such as paresthesias. In addition to experiencing pain, swelling, stasis dermatitis, and venous stasis ulceration, patients with venous hypertension associated with chronic venous compartment syndrome have been noted to have muscle atrophy and fatty degeneration on computed tomography scans.[2,10] These changes are believed to be due to chronic ischemia, necrosis, and glycogen deficiency.[11] These radiographic changes were found to be reversible when the chronic venous compartment syndrome was surgically treated.[10]

Engelbert and Turnipseed[2] have previously described a patient with a history of deep venous thrombosis and post-thrombotic syndrome with posterior calf claudication and swelling. Calf compartment pressures in the posterior superficial compartment were found to be elevated, indicative of venous hypertension. The authors performed a superficial posterior compartment fasciectomy with successful resolution of symptoms and reduction in the calf compartment pressures. Although no postoperative complications were reported in their experience, open fasciectomy can potentially be associated with complications in a leg with venous insufficiency. Use of minimally invasive compartment release techniques may offset some of these potential complications.[12,13] In another report from Turnipseed et al,[3] use of open fasciectomy in patients with venous insufficiency and CCS resulted in a complete resolution of symptoms in 66% of patients.

Table VII. Logistic regression analysis using change in compartment pressure as dependent variable

Predictors	Odds ratio	95% Confidence interval	*P* value
Sex	1.5	0.5-4.9	.5
BMI ≥30 kg/m^2	0.6	0.2-2.1	.4
Lymphedema	2.8	0.9-8.1	.06

BMI, Body mass index.

Table VIII. Logistic regression analysis using presence of lymphedema as dependent variable

Predictors	Odds ratio	95% Confidence interval	*P* value
Sex	0.3	0.9-1.1	.08
BMI ≥30 kg/m^2	3.6	0.9-13.4	.05
Change in compartment pressure	2.8	0.9-8.9	.07

BMI, Body mass index.

Endovenous stenting and hyperdilation are minimally invasive endovascular techniques with minimal morbidity and expedited recovery time. We did not observe any complications in our subset of patients and found the procedures to be technically successful. Similar to fasciectomy, these techniques appeared to result in improvement of venous hypertension in the extremity by reducing upstream venous resistance. Minimally invasive interventions, such as hyperdilation or endovenous stenting, may be considered in the treatment of chronic venous compartment syndrome before open fasciectomy. However, open surgical fasciectomy is likely to be associated with fewer symptom recurrences compared with other approaches as it probably addresses the very primary pathologic change underlying the compartment syndrome. We have previously shown the role of iliac venous stenting in the management of patients with combined outflow venous obstruction and deep reflux. In the majority of these patients, performance of stenting provided adequate symptomatic relief and "stabilized" the reflux parameters without the need for additional open procedures, such as valve reconstruction, to correct deep reflux.[14] The mechanism underlying the reduction in compartment pressure appears to be reduction of the venous resistance after hyperdilation or new stent placement. Measurement of compartment pressure in the same subset of patients in the future will be helpful to see whether the effect is sustained or whether additional procedures,

such as fasciectomy, may be needed to address other contributing factors, such as fascial fibrosis.

Baseline compartment pressures were noted to be lower in the subset of patients who had a prior history of venous stenting. Hyperdilation in these patients was noted to result in a significant improvement of the calf pump ejection fraction. In the patients receiving new stents, the calf pump ejection fraction did show a trend toward improvement, but it did not reach statistical significance. In the hyperdilation group, the baseline pressure and postintervention pressure were lower compared with the subset of patients who had new stents placed in the native iliofemoral venous system. The calf pump is subject to the pressure of the surrounding tissues as well as the upstream venous resistance. Because hyperdilation patients appeared to have a lower venous resistance by virtue of already having a history of venous stenting, it is possible that this was the likely reason for the greater improvement seen in the calf pump ejection fraction in this particular subset of patients.

The posterior superficial compartment in the calf was used for compartment pressure measurement in all patients because of safe and easy access. Blind transcutaneous compartment pressure measurement in the deep posterior compartment of the calf has not been advocated because of the potential for injury to important neurovascular structures.[3]

Study limitations. The main limitations of the study include the retrospective nature, small sample size, single-center location, and relatively short median follow-up. The compartment pressure was measured in only one compartment of the extremity because of ease of access and potential safety for the deeper neurovascular bundle. For chronic exertional compartment syndrome, most studies have measured pressure in the anterior or posterior deep compartment. For venous CCS, prior publications have used the posterior superficial compartment for pressure measurement. In addition, the compartment pressure was measured only with the patient in the supine position at rest. This may limit the applicability of the study to all patients with venous claudication.

CONCLUSIONS

Deep venous intervention in the form of hyperdilation or endovenous stent placement resulted in symptomatic improvement and reduction of compartment pressure of the extremity undergoing intervention.

AUTHOR CONTRIBUTIONS

Conception and design: TS, SR
Analysis and interpretation: TS, AK, SR
Data collection: TS, AK, SR
Writing the article: TS, AK, SR
Critical revision of the article: TS, SR
Final approval of the article: TS, AK, SR
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