Efficacy of balloon venoplasty alone in the correction of nonthrombotic iliac vein lesions

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ABSTRACT

Objective: Iliac vein stenting of nonthrombotic iliac vein lesions is an evolving treatment course for management of chronic venous insufficiency. To characterize these lesions, we examined our experience treating these lesions with balloon venoplasty before stenting.

Methods: A retrospective analysis was performed to study all patients who underwent venograms with venoplasty and stenting of iliac veins from February 2013 to July 2016. All patients included in the study were treated with a trial conservative management for 3 consecutive months before venogram and, if indicated, venoplasty was performed. If a greater than 50% reduction in cross-sectional area or diameter was observed on intravascular ultrasound examination, the stenotic area was treated with balloon angioplasty, sized to nonstenotic distal vein segment (range, 10 × 40 mm to 16 × 60 mm). Intravascular ultrasound examination was also used to measure the area of stenotic iliofemoral veins before and after balloon angioplasty.

Results: A total of 1021 venograms with venoplasty and stenting of iliac veins were performed in 713 patients from February 2013 to July 2016. The mean age of the study population age was 64.88 years (range, 21-99 years; standard deviation [SD], 14.57), with 451 female and 262 male patients. Before angioplasty, the mean cross-sectional stenotic area was 67.97 mm^2 (range, 6-318 mm^2; SD, 34.87). After balloon angioplasty, the mean stenotic area increased to 78.80 (range, 6-334 mm^2; SD, 44.50; $P < .001$). The targeted stenotic areas were categorized into three categories: group A, increased (>10% of baseline before venoplasty); group B, decreased (<10% of baseline), and group C, no area change (±10% of baseline). In 500 limbs (48.9%), the stenotic areas improved after venoplasty (average 36.99%), with a prevenoplasty average area of 60.81 mm^2 (SD, 32.80 mm^2) and a postvenoplasty average of 96.52 mm^2 (SD, 49.85 mm^2). In 294 limbs (28.8%), the area decreased (average 28.90%), with a prevenoplasty average area of 76.43 mm^2 (SD, 38.80 mm^2) and a postvenoplasty average of 53.22 mm^2 (SD, 26.61 mm^2). There were 227 patients (22.2%) who had the same area before and after venoplasty. Left-sided lesions had a greater increase in area than right-sided lesions (51.3% vs 46.2%, respectively; $P = .048$). No significant correlation of stenotic area response with age, presenting symptoms of Clinical, Etiology, Anatomy, and Pathophysiology (C2-C6), gender, or location of targeted lesion was observed.

Conclusions: Our data show there is a highly variable response after venoplasty of stenotic area of nonthrombotic iliac vein lesions. Balloon venoplasty showed greater improvement in improving the area of stenotic left-sided lesions. However, stenting of the lesions should be performed routinely owing to recoil and spasm in lesions. (J Vasc Surg: Venous and Lym Dis 2019;7:665-9.)

Keywords: Iliac vein stenosis; Iliac vein stenting; Balloon angioplasty; May Thurner syndrome; Venoplasty

Over the last two decades, balloon venoplasty and iliac vein stenting has become an evolving treatment option in the management of chronic venous insufficiency (CVI) secondary to iliac vein obstruction. Through various retrospective and prospective trials, iliac vein stenting has proven to be a safe and effective procedure, and has replaced open surgery as a primary intervention.[1-4] Although superficial venous reflux and post-thrombotic syndrome (PTS) have historically been thought to be the major contributors of venous disease, the use of intravascular ultrasound (IVUS) examination has led to the discovery that a high percentage of patients with CVI have nonthrombotic iliac vein lesions (NIVLs) as the major factor contributing to their symptoms.[5] NIVLs, such as the classically described May-Thurner syndrome, are typically due to extrinsic compression of the iliofemoral veins by an adjacent iliac artery, but may also be due impingement from nonvascular structures such as lymph nodes, tumors, and musculature.[6]

Previous investigations by Raju et al[5] have established the pathologic role of NIVLs in CVI, as evidenced by the excellent therapeutic response in patients after stent

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placement. It has been suggested that NIVLs are permissive lesions that become symptomatic in patients with concomitant reflux or other pathologies including trauma, cellulitis, distal thrombosis, or secondary lymphatic obstruction.[5] Approximately 75% of limbs with NIVLs treated with balloon dilatation and stent placement experienced excellent outcomes, with 67% of population showing healed ulcers at 2.5 years of follow-up.

One of the motivations of this study was to address the oft carried notion that iliac vein stenosis carries the same pathophysiologic characteristics of lower extremity arterial occlusive disease. A local insurance carrier required that our group perform balloon venoplasty before attempting iliac vein stenting; therefore, the objective of our study was to determine the effectiveness of performing balloon venoplasty on iliac vein stenoses before stenting in the treatment of NIVLs.

ARTICLE HIGHLIGHTS

- **Type of Research:** Single-center, retrospective cohort study
- **Key Findings:** Balloon dilatation of iliac veins alone did not reliably reduce stenosis secondary to nonthrombotic iliac vein lesions in 713 patients.
- **Take Home Message:** In patients with iliac vein obstruction secondary to nonthrombotic iliac vein lesions, balloon venoplasty alone should not be performed and stents should be used for effective treatment.

METHODS

A retrospective review of all patients who underwent venograms, venoplasty, and stenting of iliac veins from February 2013- July 2016 was performed. Institutional review board approval for this study was granted as outlined by the principles set by the Declaration of Helsinki. Informed consent was waived for this investigation, because the study was of minimal risk and the data were blinded and retrospective.

All patients included in the study were treated with a trial conservative management for 3 consecutive months, consisting of compression stockings, nonsteroidal anti-inflammatory drugs, and leg elevation, before interrogation of the iliofemoral veins with venography and IVUS examination was considered. Our study included only patients who had NIVLs, as evidenced by diagnostic IVUS measurements. If the patient had a thrombotic or PTS lesion such as fibrosis or synechiae on examination, they were excluded from the study. Each patient's treated limb was classified using the presenting symptoms of Clinical, Etiology, Anatomy, and Pathophysiology (CEAP) classification, from C2 to C6.[7]

All procedures were performed in an American Association for Accreditation of Ambulatory Surgical Facilities-accredited, office-based surgical suite by three board-certified physicians. After consent was obtained, some patients received a preoperative oral 5-mg dose of diazepam to reduce the anxiety and pain associated with the procedure. Patients were then placed in the supine position, and the ipsilateral groin was prepped and draped in the typical sterile fashion. All patients then underwent ultrasound-guided venipuncture under local anesthesia with 1% lidocaine. Access was obtained via the ipsilateral femoral or common femoral vein using a single-entry needle. A 10F sheath was then inserted through the femoral vein and confirmed via fluoroscopy. Heparin was not administered routinely during any part of the procedure. As mentioned, all patients included in the study were initially screened with contrast venography and IVUS examination to rule out thrombotic lesions. The use of contrast was minimal, with 20 mL used before the venoplasty and 20 mL used after the venoplasty. Intraoperatively, IVUS examination was used to measure and record the area of stenotic iliofemoral veins before angioplasty. Both contrast venography and IVUS examination were used to exclude thrombotic and post-thrombotic lesions. The 15 mHz Atlantis IVUS catheter (Boston Scientific, Marlborough, Mass) was used to evaluate and measure the cross-sectional area of the veins at three separate points during the procedure: before venoplasty, after venoplasty, and after stenting.

The iliofemoral veins were sequentially measured. The measurement of stenosis was compared with the adjacent nonstenotic distal segment. If a greater than 50% reduction in cross-sectional area or diameter was observed on IVUS, the stenotic area was treated with balloon venoplasty (Charger XXL, Boston Scientific), sized to a nonstenotic and nondilated distal vein segment (range, 10×40 to 16×60 mm). We use both cross-sectional area and diameter reduction in our determination of whether to stent or not, because area reduction may not be reliable in certain instances. For example, a very narrowly compressed or pancaked lesion may have sufficient area when measured, but a very small diameter (such as <2 mm) would not be conducive to flow. IVUS examination was also used to measure the area of stenotic iliofemoral veins after balloon dilatation.

The stenotic areas were categorized into three groups: group A included an increase in area (by $>10\%$ of baseline before venoplasty), group B included a decreased area ($<10\%$ of baseline), and group C with no change compared with baseline stenosed area. The locations of the stenosis were classified as distal inferior vena cava, common iliac vein (proximal, mid, and distal), external iliac vein (proximal, mid, and distal), and common femoral vein (proximal, mid, and distal). All patients included in this study with a 50% or greater decrease in cross-sectional area or diameter, when compared with a nondiseased neighboring vein segment, received

Table. Maximal area of stenosis identified via intravascular ultrasound (IVUS)

Location of stenosis	No. (%)
Inferior vena cava (distal)	1 (0.1)
Proximal common iliac vein	281 (27.5)
Mid common iliac vein	190 (18.6)
Distal common iliac vein	47 (4.6)
Proximal external iliac vein	199 (19.5)
Mid external iliac vein	220 (21.6)
Distal external iliac vein	40 (3.9)
Proximal common femoral vein	27 (2.6)
Mid common femoral vein	17 (1.6)
Distal common femoral vein	0

iliac vein stenting after balloon dilatation measurements were documented. Wallstents (Boston Scientific) were used, in diameters ranging from 14 to 18 mm and lengths ranging from 40 to 90 mm. The length and diameter of stent used was determined based on the dimensions of stenosis measured with IVUS.

Postoperatively, patients were prescribed a daily 75-mg dose of clopidogrel for 3 months, unless they were already on another antithrombotic protocol. If patients were on any other antiplatelet agent, this agent was replaced with clopidogrel for 3 months. No aspirin was prescribed after completion of the 3-month course of clopidogrel. Patients were followed with a physical examination and duplex ultrasonography within the first week of intervention, then every 3 months for the first year after the intervention.

Clinical data were entered in a single-center registry using Microsoft Excel 2017 (Microsoft Corp., Redmond, Wash) after a retrospective chart review of a patient's electronic medical records and procedural details including vein measurements analysis was performed. Statistical analysis was performed using the Student *t*-test, Fisher's exact test, and analysis of variance using IBM SPSS Statistics version 23 (IBM, Armonk, New York). The coefficients and *P* values for each vein were also interpreted using the ordinary least squares approach to look for significant association of stenosed area response with age, gender, laterality, CEAP score, and location of targeted lesion. Any result with a *P* values of less than .05 was considered statistically significant.

RESULTS

Our retrospective analysis included a total of 1021 venograms performed with venoplasty and stenting of iliac veins in 713 consecutive patients from February 2013 to July 2016. The mean age of the study population age was 64.9 years (range, 21-99 years; SD, 14.57 years), with 451 females and 262 male patients. Among them, 466 (45.6%) had right-sided lesions and 555 (54.4%) had left-sided lesion. The limb treated in each procedure was classified using the CEAP classification as: C2 (n = 75), C3 (n = 444), C4 (n = 350), C5 (n = 81), and C6 (n = 67). The location of maximal stenosis for each patient has been summarized in the Table.

The average cross-sectional stenotic area of before angioplasty was 67.97 mm^2 (range, 6-318 mm^2; SD, 34.87 mm^2). The postballoon average stenotic area was 78.80 mm^2 (range 6-334 mm^2; SD, 44.50 mm^2; $P < .001$). The stenotic areas were categorized into three categories: group A, improvement of stenosis (>10% of baseline before venoplasty), group B, worsening of stenosis (<10% of baseline), or group C, no area change (±10% of baseline). In 500 limbs (48.9%), the stenotic areas increased after venoplasty (average of 36.99%), with a prevenoplasty average area of 60.81 mm^2 (SD, 32.80 mm^2) and a postvenoplasty average of 96.52 mm^2 (SD, 49.85 mm^2). In 294 limbs (28.8%), the area decreased (average of 28.90%, with a prevenoplasty average area of 76.43 mm^2 (SD, 38.80 mm^2) and a postvenoplasty average of 53.22 mm^2 (SD, 26.61 mm^2). There were 227 patients (22.2%) who had the same area before and after venoplasty. Left-sided lesions had a greater increase in area than right-sided lesions (51.3% vs 46.2%; $P = .048$). No significant correlation of stenotic area response with age, presenting CEAP classification, gender, or location of targeted lesion was observed.

DISCUSSION

CVI is the most common vascular disease in the United States and accounts for an estimated $1 billion healthcare costs annually.[8-10] Iliac vein stenting has become an increasingly investigated treatment modality, with high levels of success and symptom improvement; however, the technical aspects of the procedure vary highly between providers.[1-4] Furthermore, the technical specifications, indications for stent placement, and perioperative protocol for iliac vein lesions attributed to NIVLs and PTS have yet to be formally differentiated.

In this study, we focused our attention to the role and effect of performing a balloon venoplasty before iliac vein stent placement for the correction of NIVLs. A local insurance carrier had required our group to perform balloon venoplasty before the placement of iliac vein stents in patients with known area reductions on IVUS examination. We believe this mandate was in part owing to the widely carried misconception that arterial and venous stenoses are similar, both in pathophysiology and response to treatment. The primary etiology of arterial stenosis is atherosclerosis, whereas the primary etiology of a NIVL is external compression, most commonly by an adjacent artery.[5] Balloon angioplasty of arterial lesions has well documented success rates[11]; however, the effect of balloon venoplasty alone on iliac vein stenoses has not been reported previously.

Although in 49% of procedures balloon dilatation relieved a previously stenotic area, there was a highly variable response to balloon venoplasty, with 22% of procedures demonstrating no change and 29% of procedures resulting in a worsening of cross-sectional area. This decrease in area could potentially be explained by elastic recoil or spasm of the vessel wall upon dilatation. Regardless of the etiology, these results question the need for routine balloon dilatation before stent placement. Although 49% of venoplasties resulted in a greater than 10% increase in area, these results are most likely transient owing the nature of NIVLs. Whereas balloon angioplasty of an atherosclerotic vessel increases luminal area secondary to controlled plaque injury, balloon dilatation of NIVLs does not permanently change the position of an extraluminal entity such as an adjacent artery, but may temporarily push it out of place and, therefore, transiently increase the vein area and diameter.

Our highly variable results of venoplasty before stenting mirror other investigations involving balloon dilatation of stenotic venous segments. One study involving balloon venoplasty of the superior vena cava (SVC) secondary to pacemaker-induced SVC syndrome resulted in restenosis within several days of the original procedure, whereas another investigation reported that balloon venoplasty resulted in resolution of symptoms and radiologic evidence of SVC patency at 6 months.[12,13] Wisselink et al[14] found that a single balloon dilatation intervention of the SVC, innominate, subclavian, and axillary veins resulted in significantly higher rates of symptom recurrence when compared with operative reconstruction.

Furthermore, a recent investigation by our group has shown that it is unnecessary to balloon dilate iliac vein stents after deployment when attempting to correct iliac vein stenosis secondary to NIVLs.[15] From a practical standpoint, balloon dilatation is a resource-intensive practice that increases total case and fluoroscopy time, radiation exposure to both providers and patients, and increases costs secondary to balloon and insufflator usage.

The high volume of procedures included this study is predicated on the treatment trends of our practice. During the time period of data collected for this investigation, iliac vein stenting was the primary modality of intervention used to treat CVI when conservative therapy failed. We have found success in treating patients with venous symptoms refractory to conservative therapy in most age groups, especially the elderly population. When patients are functional, ambulating, and debilitated by their CVI symptoms, iliac vein stenting has proven safety and efficacy, even in octogenarians and nonagenarians.[16,17] However, owing to the lack of efficacy observed by our group, C2 disease is no longer considered an indication for iliac vein interrogation. In general, our indications include persistence of symptoms after 3 months of conservative management in patients 40 years of age and older with C3 disease or higher.

The limitations of our study are consistent with its single-center, retrospective methodology. Only patients with NIVLs were included in analysis, so the efficacy of prestent balloon dilatation cannot be assessed in those with post-thrombotic iliac vein stenosis. Owing to the prestenotic dilatation seen with NIVLs, determination of a normal adjacent vein segment to use as a standard when comparing the area or diameter of a stenotic region can be subjective. Measurement of the segment just distal to the stenosis was not performed, because these dilated vein segments are also considered diseased. Each surgeon's determination of which vein segment is healthy is certainly a limitation in most studies using IVUS-measured areas and diameters as indications for stent placement. Furthermore, owing to the retrospective nature of this investigation, there are no data available to compare the efficacy of stenting after balloon venoplasty vs no balloon venoplasty. However, we believe the large size of our patient cohort portends a high statistical power and that the measurement accuracy of IVUS confirms the lack of effectiveness of prestent balloon venoplasty in the correction of NIVLs.

CONCLUSIONS

Our data show there is a highly variable response after balloon venoplasty of stenotic area of NIVLs. Left-sided stenotic lesions showed a greater improvement in increasing the area of stenotic lesions after balloon dilatation alone. However, there is a need for stenting of all NIVLs owing to an unintended chance of recoil and spasm, and the fact that balloon dilatation alone will not eliminate the external compression responsible for these lesions.

AUTHOR CONTRIBUTIONS

Conception and design: AA, JC, YO, SR, NM, AH, EA
Analysis and interpretation: AA, JC
Data collection: AA, PK, YO
Writing the article: AA, JC, AH
Critical revision of the article: AA, JC, PK, YO, SR, NM, AH, EA
Final approval of the article: AA, JC, PK, YO, SR, NM, AH, EA
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