Impact of degree of stenosis in May-Thurner syndrome on iliac vein stenting

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ABSTRACT

Objective: May-Thurner syndrome (MTS) patients with lifestyle-limiting symptoms undergo stenting of the iliac vein for relief of compressive disease. The impact of degree of stenosis on clinical symptoms and outcomes after stenting is unknown and examined in our study.

Methods: Retrospective review of contemporaneously entered data of 202 patients who underwent stenting for MTS between 2005 and 2011 was performed. Classification into three groups based on luminal area obtained by intraoperative intravascular ultrasound interrogation of the involved femoroiliac segments was carried out. Normal luminal diameters and areas were defined as 12 mm and 125 mm², 14 mm and 150 mm², and 16 mm and 200 mm² in the common femoral, external iliac, and common iliac veins, respectively. Mild (<60%), moderate (60%-89%), and severe (>90%) compression groups were defined using the normal values noted previously and observed after stenting to evaluate outcomes. Kaplan-Meier analysis was done to assess primary, primary assisted, and secondary patencies. Visual analog scale for pain scores, grade of swelling, and Venous Clinical Severity Score (VCSS) before and after stenting at 6, 24, and 48 months were analyzed using paired t-test and Tukey test. Logistic regression was used to gauge the impact of multiple variables including degree of stenosis on stent reintervention.

Results: There were 55 patients who had mild, 87 patients who had moderate, and 60 patients who had severe iliac vein compression. Baseline demographic characteristics and comorbidities were similar across all groups. In addition, there was no statistically significant difference in median baseline visual analog scale score, grade of swelling, and VCSS among the groups. Compression was treated with angioplasty and stenting encompassing all areas of disease as determined by intravascular ultrasound. Stent technique involved use of Wallstent (Boston Scientific, Marlborough, Mass) only in 183 patients and Wallstent-Z stent (Cook Medical, Bloomington, Ind) combination in the remainder. No difference in median stent patency was noted on follow-up. Clinically, at 48 months, a statistically significant recurrence of pain, swelling, and worsening of VCSS were noted in the severe stenosis group but not in the other two groups. No variable was noted to have an impact on stent reintervention.

Conclusions: Severity of MTS stenosis is not a predictor of initial clinical symptoms. Long term, patients with >90% initial MTS stenosis experience recurrence of symptoms. The degree of iliac venous stenosis does not appear to affect stent patency. Such information will help counsel patients before intervention. (J Vasc Surg: Venous and Lym Dis 2019;7:195-202.)

Keywords: May-Thurner syndrome; Nonthrombotic iliac vein lesion; Iliac compression syndrome; Iliac vein stenting; Iliofemoral stenting
Kibbe et al \cite{9} found that up to 66% of individuals have at least 25% or greater compression of the left common iliac vein. The authors noted mean compression of around 35.5%, with women having greater compression.\cite{9} In addition, multiple sites can be affected by compression, and an anatomic classification based on the nature and extent of the obstruction has recently been proposed.\cite{10} In spite of high prevalence of May-Thurner anatomy, only a small percentage go on to develop the syndrome. In fact, post-thrombotic syndrome makes up the majority of disease burden of chronic venous insufficiency due to deep venous disease. However, nonthrombotic iliac vein lesions including May-Thurner syndrome (MTS) also make a significant contribution, with MTS contributing to 15% of the disease burden in patients meritig intervention for occlusive disease.\cite{11}

Contemporary treatment of patients with MTS presenting with lifestyle-limiting symptoms is iliocaval stenting. Whereas technique and outcomes of such stenting have been described, the impact of the degree of stenosis in MTS on clinical and stent outcomes has not been explored.\cite{12-20} This study evaluates these aspects of stenting for MTS.

METHODS

Contemporaneously entered data into electronic medical records of 202 lower limbs that underwent stenting for MTS between 2005 and 2011 were analyzed. The degree of compression as ascertained by reduction in luminal area on intravascular ultrasound (IVUS) was determined. Normal luminal diameters and areas were defined as 12 mm and 125 mm$^2$, 14 mm and 150 mm$^2$, and 16 mm and 200 mm$^2$ in the common femoral, external iliac, and common iliac veins, respectively.\cite{21} Luminal compression so quantified was classified into three groups: mild ( 60% compression), moderate (60%-89% compression), and severe (>90% compression). The groups were observed after stenting to evaluate clinical and stent outcomes.

IVUS

IVUS is considered the ‘gold standard’ in the management of obstructive femoroillocaval lesions. IVUS guidance is essential for accurate diagnosis, disease characterization, intraoperative treatment guidance, and follow-up in patients with recurrent symptoms. IVUS is performed using an 8.2F, 10 MHz transducer (Philips Volcano, San Diego, Calif). Planimetric evaluation of the luminal areas of the common femoral vein, external iliac vein, and common iliac vein is made with normal luminal areas and diameters as defined before.\cite{21}

Treatment

Patients presenting with disabling symptoms including pain, swelling, hyperpigmentation, and lipodermatosclerosis suggestive of MTS underwent IVUS interrogation to confirm diagnosis and stenting once diagnosis was confirmed.

**ARTICLE HIGHLIGHTS**

**Type of Research:** Retrospective cohort study

**Key Findings:** In 202 patients who underwent iliofemoral vein stenting for May-Thurner syndrome, the severity of stenosis did not predict initial clinical symptoms or stent patency. At 48 months, patients with >90% stenosis experienced recurrence of symptoms.

**Take Home Message:** Patients with severe iliofemoral stenosis due to May-Thurner syndrome should expect some recurrence of symptoms in spite of successful stenting.

**Stent sizing.** Appropriate stent sizes were used, taking into account the element of recoil and potential for in-stent restenosis. In this regard, we used 14-mm, 16-mm, and 18-mm stent sizes in the common femoral vein, external iliac vein, and common iliac vein, respectively.\cite{21}

**Type of stent.** Either Wallstents (Boston Scientific, Marlborough, Mass) alone or more recently Wallstent-Z stent (Cook Medical, Bloomington, Ind) combination was used to treat the culprit lesion. The use of the Cook Gianturco Z stent across the iliocaval confluence was to provide additional radial force.

**Extent of stenting.** Stenting was pursued to cover all areas of disease with cranial extension across the iliocaval confluence and caudal extension into an area of good inflow.

**Technique of stenting.** Our technique of stenting described previously in multiple publications was used.\cite{13-29} In essence, it involves access to the ipsilateral femoral vein under ultrasound guidance and placement of a 11F × 10-cm sheath. Ascending venography was then performed, followed by IVUS interrogation. Once diagnosis was confirmed, predilation was carried out using 18-mm angioplasty balloons of the femorocaval segment. Stenting was then performed using Wallstent in isolation (previous technique) or Wallstent-Z stent combination (current technique). IVUS was used to decide landing zones and to confirm adequacy of apposition of the stent to the vein wall. Completion venography was finally performed to confirm adequacy of flow dynamics.

**Anticoagulation**

Anticoagulation in the perioperative period was through use of both enoxaparin and bivalirudin. Whereas enoxaparin (40 mg) was given preoperatively, bivalirudin 75 mg was given intravenously in the operating room before the start of the procedure to effectively reduce intraoperative thrombus buildup. Postoperative anticoagulation was continued with direct oral anticoagulants for a minimum of 3 months to reduce in-stent restenosis. Continuation beyond this period was dictated by clinical
presentation on follow-up, status of stent, and presence of thrombophilia. In addition, aspirin 81 mg with cilostazol 50 mg twice daily was also used unless contraindicated. The role of cilostazol is guided by its ability to suppress neointimal hyperplasia.30-33 The time to re-endothelialization after venous trauma is approximately 6 weeks.34 Cilostazol is continued for at least this duration.

Follow-up
Clinical and diagnostic imaging follow-up after stenting was pursued at 2, 4, and 6 weeks after intervention. Beyond this, follow-up with duplex ultrasound was every 3 to 6 months for the first year and 6 to 12 months subsequently. More frequent follow-up was used if clinical presentation or stent status called for it. Recurrence of disabling symptoms on follow-up was an indication to repeat IVUS interrogation and potentially to pursue angioplasty. Postoperatively, the last available clinic follow-up metric was used for postoperative outcome analysis.

Consent of the patients for the study and approval from the Institutional Review Board of the hospital were obtained.

Statistical analysis
All statistical analysis was performed using SPSS Statistics version 24 (IBM Corp, Armonk, NY). Clinical outcomes including pain, swelling, and Venous Clinical Severity Score (VCSS) were compared before and after intervention using the paired t-test and Tukey test. Patency was assessed using the Kaplan-Meier analysis. Multivariable logistic regression was used to evaluate risk factors for reintervention and symptom recurrence. P value ≤.05 was considered significant.

RESULTS
Mild compression (<60%) was noted in 55 patients (28%), moderate compression (60%-89%) in 87 patients (42%), and severe compression (>90%) in 60 patients (30%). Baseline demographic characteristics and comorbidities were similar across all groups except for predominance of left laterality (Table I). In addition, there was no statistically significant difference in median baseline visual analog scale score, swelling, or VCSS among the groups (Table II). Compression was treated with angioplasty and stenting encompassing all areas of disease as determined by IVUS and noted previously. Stent technique involved use of Wallstent only in 183 patients (91%) and Wallstent-Z stent combination in the remainder (19 [9%]). Median follow-up was 94 months.

Clinical outcomes

Pain. Pain scores were improved across all three groups at 6 months of follow-up (Table III). These scores continued to improve at 2 years. At 48 months, however, although there continued to be a statistically significant improvement compared with baseline in the mild and moderate stenosis groups, no such benefit remained in the severe stenosis group.

Swelling. Swelling was significantly improved across all three groups at 6 months after intervention and remained so at 24 months (Table III). At 48 months, only the mild and moderate stenosis groups continued to have improvement. There was no statistically significant improvement in the severe group at 48 months compared with baseline.

VCSS. The VCSS parameter was calculated without using the points attributed to use of compression stockings. At 6 months, all three groups demonstrated an improvement in the VCSS metric that remained statistically significant at 24 months (Table III). At 48 months, only the mild and moderate stenosis groups continued to have a significant improvement. There was no statistically significant difference between the baseline and 48-month VCSS metric in the severe stenosis group.

Table I. Comparison of baseline demographic variables between the three groups

<table>
<thead>
<tr>
<th>Variable</th>
<th>&lt;60%</th>
<th>60%-89%</th>
<th>&gt;90%</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>57 (17-39)</td>
<td>55 (17-83)</td>
<td>54 (20-84)</td>
<td>.25</td>
</tr>
<tr>
<td>Sex, M/F</td>
<td>13/46</td>
<td>13/73</td>
<td>10/46</td>
<td>.57</td>
</tr>
<tr>
<td>Thrombophilia</td>
<td>12 (33)</td>
<td>9 (23)</td>
<td>9 (19)</td>
<td>.32</td>
</tr>
<tr>
<td>Smoking</td>
<td>6 (17)</td>
<td>15 (29)</td>
<td>14 (33)</td>
<td>.30</td>
</tr>
<tr>
<td>Anticoagulation</td>
<td>20 (54)</td>
<td>38 (44)</td>
<td>31 (55)</td>
<td>.07</td>
</tr>
<tr>
<td>Side, left/right</td>
<td>30/29</td>
<td>75/11</td>
<td>48/8</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

Categorical variables are presented as number (%).

Table II. Impact of degree of stenosis on preintervention clinical presentation

<table>
<thead>
<tr>
<th>Variable</th>
<th>&lt;60%</th>
<th>60%-89%</th>
<th>&gt;90%</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>VAS score (pain)</td>
<td>1.25</td>
<td>1.53</td>
<td>1.72</td>
<td>.08</td>
</tr>
<tr>
<td>GS</td>
<td>1.98</td>
<td>1.79</td>
<td>1.88</td>
<td>.61</td>
</tr>
<tr>
<td>VCSS</td>
<td>5.35</td>
<td>5.13</td>
<td>5.30</td>
<td>.93</td>
</tr>
</tbody>
</table>

VCSS, Grade of swelling; VAS, visual analog scale; VCSS, Venous Clinical Severity Score.
lymphedema in the severe stenosis (≥90%) group. On univariate analysis, lymphedema was not found to be a statistically significant predictor for recurrence of symptoms. To enable adequate sample size for the stent compression variable, we compared the <90% stenosis group (n=5) with the ≥90% stenosis group (n=12). Statistically significant stent compression (P ≤ .05) occurred between 24 and 48 months across both mild to moderate (<90%) stenosis groups. Postintervention, Preintervention.

Table III. Impact of degree of stenosis on postintervention clinical presentation

<table>
<thead>
<tr>
<th>Variable</th>
<th>&lt;60% Stenosis</th>
<th>60%-89% Stenosis</th>
<th>≥90% Stenosis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>6 months</td>
<td>24 months</td>
<td>48 months</td>
</tr>
<tr>
<td>VAS score</td>
<td>Pre</td>
<td>Post</td>
<td>P</td>
</tr>
<tr>
<td>&lt;60% Stenosis</td>
<td>1.42</td>
<td>0.11</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>60%-89% Stenosis</td>
<td>1.43</td>
<td>0.25</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>≥90% Stenosis</td>
<td>1.48</td>
<td>0.31</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>GS</td>
<td>Pre</td>
<td>Post</td>
<td>P</td>
</tr>
<tr>
<td>&lt;60% Stenosis</td>
<td>2.26</td>
<td>0.68</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>60%-89% Stenosis</td>
<td>1.86</td>
<td>0.56</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>≥90% Stenosis</td>
<td>2.00</td>
<td>0.79</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>VCSS</td>
<td>Pre</td>
<td>Post</td>
<td>P</td>
</tr>
<tr>
<td>&lt;60% Stenosis</td>
<td>5.35</td>
<td>2.18</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>60%-89% Stenosis</td>
<td>5.13</td>
<td>1.65</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>≥90% Stenosis</td>
<td>5.30</td>
<td>1.86</td>
<td>&lt;.01</td>
</tr>
</tbody>
</table>

Post, After intervention; pre, before intervention.
and severe ($\geq 90\%$) groups. However, the data were inadequate (missing variables) to demonstrate a significant difference between $<90\%$ and $\geq 90\%$ stenosis groups, although it is possible that a significant difference might have been found if there had been an adequate sample size on follow-up.

Fig 1. Primary patency after iliocaval stenting for May-Thurner syndrome (MTS).

Fig 2. Primary assisted patency after iliocaval stenting for May-Thurner syndrome (MTS).
Stent outcomes

Patencies are depicted in Figs 1 to 3. There was no statistically significant difference in primary patency between mild, moderate, and severe stenosis groups. The median patencies in the three groups were 88 ± 17 months, 93 ± 13 months, and 96 ± 21 months for the mild, moderate, and severe stenosis groups, respectively (P > .05). Primary assisted patency was also not statistically significantly different across the groups (35 ± 7 months, 38 ± 6 months, and 47 ± 5 months for mild, moderate, and severe stenosis groups).

Risk factors for reintervention in MTS

Sex, age, thrombophilia, and degree of stenosis were evaluated as potential predictors for reintervention after stenting for MTS (Table IV). However, logistic regression analysis did not demonstrate a statistically significant predictor. There was no difference in the reintervention rates between the three groups. In addition, there did not appear to be a difference in reintervention rates based on nature of stenting (Wallstent alone vs Wallstent-Z stent combination) across all three groups (Table V).

DISCUSSION

Endovenous techniques have supplanted open surgery as the treatment of choice in patients with MTS presenting with disabling symptoms. Whereas better outcomes have been reported with stenting for MTS compared with stenting for post-thrombotic syndrome, it is not known whether the degree of stenosis in MTS itself has an impact on such outcomes. Such data would help provide prognosis data to patients under consideration for iliocaval stenting.

Table IV. Results of multivariable regression analysis: Predictors for reintervention

<table>
<thead>
<tr>
<th>Variable</th>
<th>OR</th>
<th>95% CI Lower</th>
<th>95% CI Upper</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td>1.3</td>
<td>0.6</td>
<td>2.8</td>
<td>.4</td>
</tr>
<tr>
<td>Age</td>
<td>0.7</td>
<td>0.5</td>
<td>1.3</td>
<td>.3</td>
</tr>
<tr>
<td>Thrombophilia</td>
<td>0.9</td>
<td>0.4</td>
<td>2.7</td>
<td>.9</td>
</tr>
<tr>
<td>Degree of stenosis</td>
<td>1.3</td>
<td>0.8</td>
<td>1.8</td>
<td>.1</td>
</tr>
</tbody>
</table>

CI, Confidence interval; OR, odds ratio.

Table V. Reintervention for Wallstent and Wallstent-Z stent combination across the three groups

<table>
<thead>
<tr>
<th>Type of stent</th>
<th>Reintervention, No.</th>
<th>&lt;60%</th>
<th>60%-89%</th>
<th>≥90%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wallstent alone</td>
<td>49</td>
<td>79</td>
<td>55</td>
<td></td>
</tr>
<tr>
<td>Wall stent reintervention</td>
<td>22</td>
<td>40</td>
<td>35</td>
<td></td>
</tr>
<tr>
<td>Wallstent + Z stent</td>
<td>6</td>
<td>8</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Wallstent + Z stent reintervention</td>
<td>5</td>
<td>8</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Total patients</td>
<td>55</td>
<td>87</td>
<td>60</td>
<td></td>
</tr>
<tr>
<td>Total reinterventions</td>
<td>27</td>
<td>48</td>
<td>37</td>
<td></td>
</tr>
</tbody>
</table>
Impact of degree of stenosis on clinical presentation and outcomes. As noted from Table II, there is no difference in the baseline clinical presentation between the groups, indicating that the degree of stenosis probably does not affect the initial clinical picture. After stenting, there is relief of symptoms across all groups until the 24-month follow-up. However, on long-term follow-up (48 months), the severe stenosis group appears to have recurrence of symptoms, including pain and swelling. There is also a decline of the VCSS metric in this group to the point of no statistically significant benefit at 48 months of follow-up. It appears that patients with severe MTS have a statistically significant recurrence of symptoms on long-term follow-up compared with the mild and moderate stenosis cohorts.

Impact of degree of stenosis on stent outcomes. On evaluation of primary, primary assisted, and secondary patencies, there does not appear to be an impact of degree of stenosis in MTS on such patencies. A statistically significant difference was not noted for patencies across the three groups. Whereas the severe stenosis group may have had recurrent symptoms, this has not come at the cost of loss of stent patency. Logistic regression was used to determine predictors for reintervention in the entire cohort. However, none of the variables examined appeared to be statistically significant predictors for reintervention. Whereas the degree of stenosis had an odds ratio of 1.3, the P value of 0.1 did not lend support to presence of an impact of such stenosis on stent reinterventions. No impact was noted on stent outcomes based on type of stenting (Wallstent alone vs Wallstent-Z stent combination), although the latter group constituted only a small number, making it difficult to draw a firm conclusion.

The degree of stenosis in MTS is a predictor for clinical recurrence of symptoms on long-term follow-up. Our hypothesis is that this symptom recurrence is due to reduction in the caliber of the stent over time in the severe stenosis group compared with the mild and moderate stenosis groups, reflecting greater extrinsic compression from a greater degree of stenosis.

CONCLUSIONS
Severity of MTS stenosis is not a predictor of initial clinical symptoms. Long term, patients with ≥90% initial MTS stenosis experience recurrence of symptoms. The degree of iliac venous stenosis does not appear to affect stent patency. Such information will help counsel patients before intervention.

AUTHOR CONTRIBUTIONS
Conception and design: AJ
Analysis and interpretation: AJ, WB, AK, SR
Data collection: AJ, WB, AK, BJ
Writing the article: AJ, WB, AK, BJ, SR
Critical revision of the article: AJ, SR
Final approval of the article: AJ, WB, AK, BJ, SR
Statistical analysis: AJ, WB, AK, BJ
Obtained funding: Not applicable
Overall responsibility: AJ

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