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Medical therapy and intervention do not improve uncomplicated isolated mesenteric artery dissection outcomes over observation alone

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ABSTRACT

Objective: Isolated dissection of the mesenteric vessels is rare but increasingly recognized. This study aimed to evaluate patient characteristics, primary treatment, and subsequent outcomes of mesenteric dissection using multi-institutional data.

Methods: All patients at participant hospitals between January 2003 and December 2015 with dissection of the celiac artery (or its branches) or dissection of the superior mesenteric artery (SMA) were included. Patients with an aortic dissection were excluded. Demographic, treatment, and follow-up data were collected. The primary outcomes included late vessel thrombosis (LVT) and aneurysmal degeneration (AD).

Results: Twelve institutions identified 227 patients (220 with complete treatment records) with a mean age of 55 ± 12.5 years. Median time to last follow up was 15 months (interquartile range, 3.8–32). Most patients were men (82% vs 18% women) and symptomatic at presentation (162 vs 65 asymptomatic). Isolated SMA dissection was more common than celiac artery dissection (n = 158 and 81, respectively). Concomitant dissection of both arteries was rare (n = 12). The mean dissection length was significantly longer in symptomatic patients than in asymptomatic patients in both the celiac artery (27 vs 18 mm; P = .01) and the SMA (64 vs 40 mm; P < .001). Primary treatment was medical in 146 patients with oral anticoagulation or antiplatelet therapy (n = 76 and 70, respectively), whereas 56 patients were observed. LVT occurred in six patients, and 16 patients developed AD (3% and 8%, respectively). For symptomatic patients without evidence of ischemia (n = 134), there was no difference in occurrence of LVT with medical therapy compared with observation alone (9% vs 0%; P = .35). No asymptomatic patient (n = 64) had an episode of LVT at 5 years. AD rates did not differ among symptomatic patients without ischemia treated with medical therapy or observed (9% vs 5%; P = .95). Surgical or endovascular intervention was performed in 18 patients (3 ischemia, 15 pain, 1 AD, 1 asymptomatic). Excluding the patients treated for ischemia, there was no difference in LVT with surgical intervention vs medical management (one vs five; P = .57).

Conclusions: Asymptomatic patients with isolated mesenteric artery dissection may be observed and followed up with intermittent imaging. Symptomatic patients tend to have longer dissections than asymptomatic patients. Symptomatic isolated mesenteric artery dissection without evidence of ischemia does not require anticoagulation and may be treated with antiplatelet therapy or observation alone. (J Vasc Surg 2017;1-7.)
Isolated mesenteric artery dissection (IMAD) is generally described as a rare but increasingly encountered vascular pathologic process. First described by Bauersfeld in 1947, the early literature showed that mesenteric artery dissections were associated with poor outcomes, with 5 of the first 11 reports progressing to bowel ischemia and death. The underlying cause of IMAD is still unknown. One hypothesis implicates the transition from a relatively fixed to an unrefixed arterial segment, causing flow stagnation and subsequent abnormal mechanical stress to the anterior arterial wall.

Recent treatment recommendations for symptomatic and asymptomatic patients vary on the basis of the experiences of individual institutions and have been supported mostly by small retrospective reviews and a few larger retrospective reviews. Suggested treatments include medical management with or without anticoagulation, surgery, and endovascular intervention. Whereas indications for immediate intervention can be self-evident, the optimal treatment is uncertain for patients with anything less than significant end-organ ischemia. This is especially the case for symptomatic patients whose pain does not quickly resolve. As such, some have tried to identify radiologic characteristics of the dissection that may better inform clinical decision-making at the time of diagnosis, such as subtyping of dissections based on morphology.

This multi-institutional study was then conducted to evaluate patient and radiologic characteristics, primary treatment, and subsequent outcomes for IMAD. Our primary outcomes of interest were late vessel thrombosis (LVT) and aneurysmal degeneration (AD) of the dissected mesenteric artery.

METHODS

This is a multi-institutional, retrospective cohort analysis of patients evaluated or treated between January 2003 and December 2015 with IMAD of the celiac axis, the superior mesenteric artery (SMA), or both vessels. Institutions were recruited through the Vascular Low Frequency Disease Consortium (University of California-Los Angeles Division of Vascular Surgery). A call for participation to institutions with an interest was sent through e-mail. Institutions expressing interest to participate were allowed into the study once they demonstrated Investigational Review Board (IRB) approval from their home institution. The IRB at the University of California, Davis approved the study protocol. The IRB waived the patient consent process because of minimal patient risk. Data were collected by each institute’s respective investigators and stored using a password-encrypted database (Velos eResearch System; Velos, Inc, Fremont, Calif) maintained by the University of California, Davis.

Inclusion criteria and patient identification. Patients were identified using the International Classification of Diseases, Ninth Revision (ICD-9) code 443.29 (dissection of other artery) while excluding codes 441.0 to 441.03 (dissection of aorta). Additional patients were identified by search of the picture archiving and communication system using search terms of “celiac dissection,” “surgical treatment,” or “superior mesenteric artery dissection,” “mesenteric artery dissection,” and “mesenteric arterial dissection.” Institutions unable to perform picture archiving and communication system search queries were allowed to enter patients on the basis of ICD-9 codes only. Patients presenting with rupture of the celiac axis, SMA were not included if there was no clear imaging demonstrating an IMAD.

Patient variables. Data collected contained patient demographics, presenting symptoms, radiographic measurements, primary treatment, and follow-up data including occurrence of LVT or AD. Patients were defined as symptomatic or asymptomatic. Symptomatic patients presented with at least one symptom of abdominal pain, nausea, or vomiting. Symptomatic patients were also broken down into those with and without evidence of intestinal ischemia on initial evaluation as determined by the participating institution’s chart review.

Treatment. Patients were classified by the primary treatment at the time the dissection was identified (medical, surgical, observation). Medical management was defined as initial treatment with antiplatelet or anticoagulation medications. Treatment was further classified as antiplatelet only, anticoagulation only, or combination treatment. The addition of new antihypertensive medications or a change in a patient’s antihypertensive medications after identification of the dissection was also collected. Surgical treatment was defined as any operation including bypass, embolectomy, patch angioplasty, or endovascular intervention.

Radiographic data. We collected data on the imaging modality used for initial diagnosis of IMAD. When available, images were reviewed for dissection length, maximal

ARTICLE HIGHLIGHTS

- Type of Research: Retrospective multicenter cohort study
- Take Home Message: Only 18 of 227 patients with superior mesenteric and celiac artery dissection underwent surgical or endovascular intervention. Symptomatic patients without gut ischemia were treated with antiplatelet therapy or observation with excellent results.
- Recommendation: The authors suggest that isolated mesenteric artery dissections in symptomatic patients should be treated with antiplatelet therapy or observation and asymptomatic patients may be observed with serial imaging.
diameter of the dissected artery, whether branches of the dissected artery were involved, and characteristics of the aorta at the origin of the dissected vessel. Dissection length was determined by centerline measurement on computed tomography (CT) at facilities with this capability. At facilities without software able to create centerline reconstruction, length was measured on coronal or sagittal CT images. For measurement on duplex ultrasound imaging, calipers were used to measure dissection length, and measurements were approximated using image ruler bar standardization. When the dissection continued into vessel branches, the length was estimated on the basis of the end point at which no further dissection could be identified. Diameter measurements were obtained from inner to inner wall to account for cases in which hemorrhage or surrounding tissue edema obscured the outer vessel wall. Imaging characteristics at the time of follow-up were collected if available. In cases in which images were not able to be reviewed, radiographic reports were used to determine measurements. Measurements were determined at the individual institutions and not at a central radiographic core laboratory.

### Follow-up
Clinical follow-up data included date of last evaluation of the patient, defined by date of last available clinic note or imaging. The occurrence of the primary outcomes, LVT and AD, was collected along with the presence of residual symptoms. AD was defined as a vessel diameter 1.5 times the normal vessel diameter. Secondary outcomes measured included death.

### Data analysis
Categorical data were described by frequency and compared using $\chi^2$ tests. Continuous variables were analyzed using Student t-test and analysis of variance. Where data were skewed, the median and interquartile range (IQR) were reported. Where data were distributed normally, mean and standard deviation were reported. LVT and AD were analyzed as separate outcomes for comparison of the primary treatment groups. Freedom from LVT or AD was determined by Kaplan-Meier estimates and adjusted to determine groupings. Freedom from LVT or AD was determined by Kaplan-Meier analysis. A P value of < .05 was considered statistically significant. All statistical analysis was performed using R software, version 3.1.2 (R Foundation for Statistical Computing, Vienna, Austria).

### RESULTS
Twelve institutions identified 227 patients from the United States ($n = 125$), Japan ($n = 73$), The Netherlands ($n = 19$), and France ($n = 10$). The mean age at diagnosis for the entire cohort was $55 \pm 12.5$ years. More patients were men (82%) and symptomatic (162 vs 65 asymptomatic). Asymptomatic patients were on average slightly older than symptomatic patients (60 vs 55 years; $P = .04$), but otherwise there were no significant differences in comorbidities between symptomatic and asymptomatic patients (Table I). Sixty-one patients (27%), including 54 symptomatic patients and seven asymptomatic patients, were transferred from an outside hospital.

#### Dissection characteristics
Isolated SMA dissection was more common than celiac artery dissection ($n = 158$ and 81, respectively; Table I). Dissection of both the SMA and celiac artery was rare ($n = 12$). Patients with dissection of both the celiac artery and SMA were symptomatic in 82% of cases. In cases in which the dissection involved only the celiac artery or the SMA, there was no difference in the proportion of patients who were symptomatic (62% vs 75%, respectively; $P = .09$). The mean dissection length was longer for the SMA than for the celiac artery (58 mm vs 23 mm; $P < .001$). The mean dissection length was significantly longer in symptomatic patients than in asymptomatic patients in both the celiac artery (27 vs 18 mm; $P = .01$) and the SMA (64 vs 40 mm; $P < .001$). In addition, symptomatic patients were more likely than asymptomatic patients to have multibranch involvement in both the celiac artery (79% vs 46%; $P = .01$) and the SMA (80% vs 61%; $P = .04$).

#### Primary treatment groups
Of the 227 patients, 220 had available treatment records; 56 (25%) were observed, 146 (64%) received medical management, and 18 (8%) underwent surgical therapy. The distribution of treatment in symptomatic and asymptomatic patients is shown in Fig 1. In patients who received medical

### Table I. Characteristics of symptomatic and asymptomatic patients with isolated mesenteric artery dissection (IMAD)

<table>
<thead>
<tr>
<th></th>
<th>Symptomatic patients ($n = 162$)</th>
<th>Asymptomatic patients ($n = 65$)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age, years</strong></td>
<td>$55.25 \pm 11.9$</td>
<td>$59.79 \pm 15.18$</td>
</tr>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>29 (18)</td>
<td>12 (18)</td>
</tr>
<tr>
<td>Male</td>
<td>131 (81)</td>
<td>52 (80)</td>
</tr>
<tr>
<td>Unknown</td>
<td>2 (1)</td>
<td>1 (2)</td>
</tr>
<tr>
<td><strong>Hypertension</strong></td>
<td>73 (45.1)</td>
<td>35 (53.8)</td>
</tr>
<tr>
<td><strong>Coronary artery disease</strong></td>
<td>15 (9.3)</td>
<td>12 (18.5)</td>
</tr>
<tr>
<td><strong>Connective tissue disorder</strong></td>
<td>3 (1.9)</td>
<td>3 (4.6)</td>
</tr>
<tr>
<td><strong>Smoking history</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current or prior</td>
<td>82 (50.6)</td>
<td>38 (58.5)</td>
</tr>
<tr>
<td>Never</td>
<td>80 (49.4)</td>
<td>27 (41.5)</td>
</tr>
</tbody>
</table>

Continuous variables are presented as mean ± standard deviation. Categorical variables are presented as number (%).

*Includes Ehlers-Danlos syndrome, antiphospholipid syndrome, polyarteritis nodosa, and rheumatoid arthritis.
management. 33 patients (23%) received oral anti-coagulation therapy, 70 patients (48%) received anti-platelet therapy, and 42 (29%) received both antiplatelet and anticoagulation. Of the 75 patients who received anticoagulation, 24 patients had only short-term intravenous anticoagulation at a mean of 4.2 days (±1.8 days). In six of these patients, intravenous heparin was used initially, but they were transitioned to dual antiplatelet therapy at discharge. In 13 patients, it was used as a bridge to anticoagulation, and in the other five patients, all medical anticoagulation and antiplatelet therapy was stopped at the time of discharge. Antihypertensive medication was started in six patients, whereas 42 patients had the antihypertensive medication changed.

Surgical intervention was the primary treatment in 18 patients (8%). The indications for intervention included intestinal ischemia (n = 6), vessel thrombosis without ischemia (n = 6), and AD (n = 6). In the 6 patients treated for ischemia, 3 patients were treated by thrombectomy and patch angioplasty, 1 underwent endarterectomy, 1 was treated by surgical bypass, and 1 patient had an uncovered self-expanding stent placed. Patients treated for thrombosis without evidence of ischemia were also treated by patch angioplasty (n = 1), surgical bypass (n = 1), patch angioplasty plus endovascular lysis (n = 1), endovascular angioplasty with (n = 1) or without (n = 1) stent placement, and endovascular lysis only (n = 1). In those treated for AD, two patients underwent surgical bypass, one patient had aneurysmorhaphy, one had an interposition graft, and two patients were treated by endovascular balloon-expandable covered stent placement.

Outcomes. In patients treated with primary surgery, LVT occurred in one patient (median, 14 months), and there were no patients with AD at an overall median follow-up of 18 months. The occurrence of LVT and AD in the medical management group was compared with the observation group, for both symptomatic and asymptomatic patients. No asymptomatic patient treated medically or observed developed LVT with a median follow-up time of 18 months (IQR, 7-45 months). Six asymptomatic patients went on to develop AD at a median follow-up time of 6.5 months (IQR, 1.0-12.1 months). Of these six patients, three had received antiplatelet therapy and three were observed (10.7% vs 8.8%; P = .99).

Of the symptomatic patients, six developed LVT after a median time of 2 months (IQR, 0.4-3.6 months; Table III). Three were dissections of the celiac artery and three were SMA dissections. Initial dissection length measurements were available in two of these patients (130 and 107 mm). For symptomatic patients without evidence of ischemia (n = 134), the incidence of LVT was not
significantly different with medical management compared with observation alone (9% vs 0%; \( P = .35 \)). For those patients treated medically (n = 113), there was no significant difference in LVT between those treated with antiplatelet plus anticoagulation and those treated with antiplatelet alone (10% vs 0%; \( P = .10 \); Fig 2; Table IV).

False lumen thrombosis was present at diagnosis in 61 patients. Of the remaining patients, 153 did not have false lumen thrombosis and 13 patients developed false lumen thrombosis at a mean of \( 6.15 \) months. In patients treated medically, there was no difference in the occurrence of false lumen thrombosis based on whether patients were treated with anticoagulation or antiplatelet therapy (\( P = .014 \)).

Occurrence of LVT in symptomatic patients without ischemia was also compared in the surgical intervention group (n = 12) and the nonsurgical treatment groups (n = 134). Again excluding patients with evidence of ischemia, there was no difference in LVT incidence in symptomatic patients between those treated with surgical intervention and those treated with nonsurgical management (8% vs 4%; \( P = .57 \)).

AD developed in 10 symptomatic patients at a median follow-up time of 10 months (IQR, 1-14 months). The mean maximal diameter of the dissected vessel at the time of diagnosis in these patients was 11.7 ± 1.8 mm compared with 11.6 ± 2.7 mm in symptomatic patients without AD (\( P = .89 \)). None of the patients had a dissection diameter >20 mm at time of diagnosis. The incidence of AD in symptomatic patients without ischemia was not significantly different with medical management (n = 113) compared with observation alone (n = 21; 9% vs 5%; \( P = .95 \)).

Ten patients died at a median of 9 months (IQR, 6-18 months). Of those 10 patients, 5 were observed, 3 were treated with anticoagulation, and 2 were treated with antiplatelet therapy.

Table III. Presentation, treatment, and time to outcome for patients who developed late vessel thrombosis (LVT)

<table>
<thead>
<tr>
<th>Age, years/sex</th>
<th>Presenting symptom</th>
<th>Surgical intervention?</th>
<th>Treatment received</th>
<th>Months to LVT</th>
</tr>
</thead>
<tbody>
<tr>
<td>42/male</td>
<td>New-onset abdominal pain</td>
<td>No</td>
<td>Dual therapy</td>
<td>1.1</td>
</tr>
<tr>
<td>71/male</td>
<td>New-onset abdominal pain</td>
<td>Yes</td>
<td>Surgical bypass</td>
<td>2.4</td>
</tr>
<tr>
<td>75/male</td>
<td>New-onset abdominal pain</td>
<td>No</td>
<td>Anticoagulation</td>
<td>1.5</td>
</tr>
<tr>
<td>69/female</td>
<td>New-onset abdominal pain</td>
<td>No</td>
<td>Anticoagulation</td>
<td>18.0</td>
</tr>
<tr>
<td>55/male</td>
<td>New-onset abdominal pain</td>
<td>No</td>
<td>Dual therapy</td>
<td>3.0</td>
</tr>
<tr>
<td>42/male</td>
<td>New-onset abdominal pain</td>
<td>No</td>
<td>Dual therapy</td>
<td>1.0</td>
</tr>
</tbody>
</table>

Dual therapy consisted of an antiplatelet in combination with an anticoagulant.

![Fig 2. Late vessel thrombosis (LVT) in symptomatic patients comparing anticoagulation with antiplatelet therapy.](image_url)
**DISCUSSION**

This study reports a large series of patients with IMAD identified during an 11-year period when abdominal CT imaging was routinely used for diagnosis and patients were treated with medical management, surgical intervention, or observation. We found that when they were observed or managed with antiplatelet medications, patients with IMAD without evidence of ischemia were not at increased risk of LVT compared with treatment with anticoagulation. In addition, symptomatic patients tended to have longer dissections than asymptomatic patients. Finally, asymptomatic IMAD patients can be observed and followed up with intermittent imaging.

Despite relatively few reports of asymptomatic IMAD compared with symptomatic IMAD in the literature, nearly a third of total patients identified in this study were asymptomatic. Most were simply observed and none developed late thrombosis, whereas six progressed to AD. These findings are similar to other reports in the literature. A systematic review conducted by Garrett found that asymptomatic patients with IMAD of the SMA were more likely than symptomatic patients to be successfully treated with medical therapy alone. He found that failure rate was 3% for asymptomatic patients compared with 16% for symptomatic patients. Our findings suggest that patients with uncomplicated, asymptomatic IMAD may not even benefit from medical management for prevention of thrombosis or aneurysm. Our median follow-up time in asymptomatic patients was 18 months. Because it is still unclear whether these patients are at risk for AD further out, we recommend that asymptomatic patients undergo intermittent repeated imaging at 6 and 12 months after diagnosis to ensure that they do not develop AD.

Symptomatic patients in our study had longer dissection lengths, both of the celiac artery and of the SMA. Similar findings have been reported in prior smaller studies of SMA dissections. Park et al found that the average length of SMA dissection in a group of 12 asymptomatic patients was 44 mm. In our group of 65 asymptomatic patients, we found that the average SMA dissection length was even somewhat shorter at 40 mm. Overall, we observed that the average SMA dissection length was 58 mm, which is similar to reported SMA dissection lengths ranging from 4 to 7 cm. In our study, dissection length data were available in two of six patients who went on to develop LVT. Both had SMA dissections roughly twice the average length, suggesting that long-segment dissections may be at higher risk for LVT, need more careful monitoring at 6-month intervals during the first year after diagnosis, and possibly need more intensive treatment.

The small amount of literature on IMAD suggests that medical therapy alone is all that is needed. However, what constitutes optimal medical therapy is unknown. In general, some combination of antihypertensive, anticoagulation, or antiplatelet drug therapy is recommended. Many authors reported good outcomes using anticoagulation therapy and some have called for anticoagulation as first-line therapy. We found that in symptomatic patients without evidence of ischemia, there was no significant difference in occurrence of LVT or aneurysm in patients treated with medical management vs observation alone. Furthermore, we found that there was no significant difference in LVT in patients treated with anticoagulation plus antiplatelet therapy vs only antiplatelet therapy. This suggests that anticoagulation is not needed as first-line therapy for symptomatic IMAD, and instead these patients may be treated with antiplatelet therapy or observed. However, this may not be the case in patients with long-segment artery dissections with branch involvement.

Surgery was the primary treatment in only 18 patients, 16 of whom were symptomatic with new-onset severe abdominal pain and what at the time was believed by the physician to be signs of mesenteric ischemia. All patients were treated with surgery, with one patient having lysis in addition to surgery. We hypothesize that endovascular therapy is used less in this population of patients because of the long length of the dissection and the involvement of branches with this disease. This is supported by the higher number of patients who underwent patch angioplasty as the surgical treatment of choice. However, given the limited numbers, we are unable to recommend one surgical or endovascular treatment over the other.

One of the main limitations of this study is its retrospective design, which prevents capture of all IMADs. Patients who presented with abdominal pain but were not imaged using CT or duplex ultrasound would not have been included in this study. Second, despite a large number of patients, the number of primary outcomes was relatively small. This made it difficult to detect risk factors for LVT or aneurysm and could have led to type II error in comparing outcomes in different treatment groups. We also did not collect data beyond the primary end point regarding how patients with LVT or AD were

**Table IV.** Cox proportional hazards model of patients’ characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>HR</th>
<th>95% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>1.07</td>
<td>0.96-1.12</td>
<td>.18</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female Referent</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>0.61</td>
<td>0.05-7.5</td>
<td>.70</td>
</tr>
<tr>
<td>Current tobacco use</td>
<td>3.7</td>
<td>0.39-34</td>
<td>.25</td>
</tr>
<tr>
<td>Drug use</td>
<td>2.01</td>
<td>0.08-52</td>
<td>.67</td>
</tr>
</tbody>
</table>

CI: Confidence interval. HR, hazard ratio. P < .05 considered statistically significant.
treated. The rationale for this was a balance between asking multiple sites to collect an enormous amount of retrospective data and limiting the data collection to answer a specific question regarding primary treatment of patients with IMAD. Finally, the extreme form of this disease would likely present with mesenteric artery thrombosis or rupture. These patients also would not be included in the cohort because of how we identified patients. For this reason, we are unable to identify or to make recommendations on the characteristics that may lead to the worst outcomes for patients with initial IMAD.

CONCLUSIONS

Asymptomatic patients with IMAD may be observed and followed up with intermittent imaging. Symptomatic patients tend to have longer dissections than asymptomatic patients. Symptomatic IMAD without evidence of ischemia does not require anticoagulation and may be treated with antiplatelet therapy or observation alone.

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AUTHOR CONTRIBUTIONS

Conception and design: JL, MH, PL
Analysis and interpretation: JL, MH
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Final approval of the article: JL, HO, NF, PB, DN, SZ, AV, RG, KCO, SS, NS, AR, NG, MHL, WG, MH, PL
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