

MHIF FEATURED STUDY:
HITSOVA

OPEN AND ENROLLING:
Please Refer Patients!

CONDITION:

Heparin Induced
Thrombocytopenia

PI:

Nedaa Skeik, MD

RESEARCH CONTACTS:

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OBJECTIVE:

Prove that danaparoid use is not inferior to argatroban in terms of efficacy in HIT

ENDPOINTS:

1. Approximately Day 14 end study medication
2. Subject considered a treatment responder if none of the following occur @D44
 - New or extended venous and/or arterial thrombosis, including gangrene/skin necrosis
 - All-cause mortality
 - Unplanned amputation, including ischemic gut resection

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DESCRIPTION: Open-Label, Randomized, Active Controlled, Multi-Centre Phase 3 Study to Evaluate the Safety and Efficacy of Danaparoid vs Argatroban in Treatment of Subjects with Acute HIT (HITSOVA study)

CRITERIA LIST/ QUALIFICATIONS:

Inclusion

Males or females aged ≥ 2 weeks

Subjects with suspected HIT by 4Ts of >3 and with reduction of platelet count of $\geq 30\%$ at either:

- a) Between Day 4 and 14 of the start of heparin exposure **OR**
- b) At Day 1 of heparin exposure with pre-treatment with heparin within the last 30 days

Have adequate renal function: Glomerular filtration rate ≥ 15 mL/min/1.73 m²

Exclusion

- Cardiac surgery within 44 days
- Intra-aortic balloon pump or VAD
- Life expectancy less than study duration of 44 days
- Spinal/epidural access within past 48 hrs
- Severe hepatic impairment (Child-Pugh Class C)
- Active bleeding
- Hemorrhagic cerebrovascular accident within previous 3 mos.
- Severe, uncontrolled hypertension ($>180/110$ mmHg)
- Long-term (>3 wks) HD or continuous renal replacement

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Minneapolis Heart Institute Foundation® Cardiovascular Grand Rounds

Title: Non-Atherosclerotic Vasculopathies

Speaker: Nedaa Skeik, MD, FACC, FACP, FSVM

Section Head, Vascular Medicine

Medical Director, Vein Center

Medical Director, Anticoagulation and Thrombophilia Clinic

Medical Director, Vascular Lab

Minneapolis Heart Institute® at Abbott Northwestern Hospital

Date: January 13, 2020

Time: 7:00 - 8:00 AM

Location: Minneapolis Heart Institute Building, Suite 100, Learning Center

OBJECTIVES

At the completion of this activity, the participants should be able to:

1. Identify abdominal non-atherosclerotic arterioapthies
2. Analyze different underlying etiologies
3. Determine differential diagnoses and management planning

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Moderator(s)/Speaker(s)

Dr. Nedaa Skeik has disclosed the following commercial interests: Consultant- Boston Scientific; Speaker’s Bureau- Janssen, Boehringer Ingelheim, Pfizer, Bristol-Myers Squibb

Planning Committee

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Non-Atherosclerotic Abdominal Vasculopathies


Nedaa Skeik, MD, FACC, FACP, FSVM, RPVI
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Section Head, Vascular Medicine
Medical Director, Thrombophilia/Anticoagulation Clinic
Medical Director, Vein Practice
Medical Director, Vascular Laboratory
Minneapolis Heart Institute® Abbott Northwestern Hospital




Disclosures





Consulting and speaking for Pfizer, BMS, J&J, B.I. and BSC:
Not relevant to this talk




No financial conflict related to this talk





Cases were modified for education purposes





Learning Objectives






 Discuss different non-atherosclerotic abdominal vasculopathies, *case presentations*



 Cover underlying etiologies (e.g. FMD, SAM, connective tissue disorders, vasculitis,..)

 Provide some tools to help with differential diagnoses

 Summarize management planning and outcome



 Share our center experience







Background

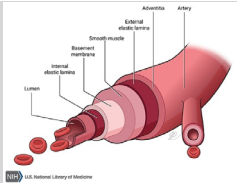
- **Problem:** Mesenteric and or renal artery dissection, aneurysm, stenosis, thrombosis or vasculitis
- **Epidemiology:** Very rare with great clinical significance. Very scarce literature!
- **Presentation:** Incidental → arterial rupture and life-threatening bleed!
- **Diagnosis/Management:**
 - No consensus on diagnostic process, management or follow up strategy
 - Hard to make a differential diagnosis (e.g. FMD, SAM, vasculitis..)
 - Management can be very challenging
- **Outcome:** Varies based on underlying etiology





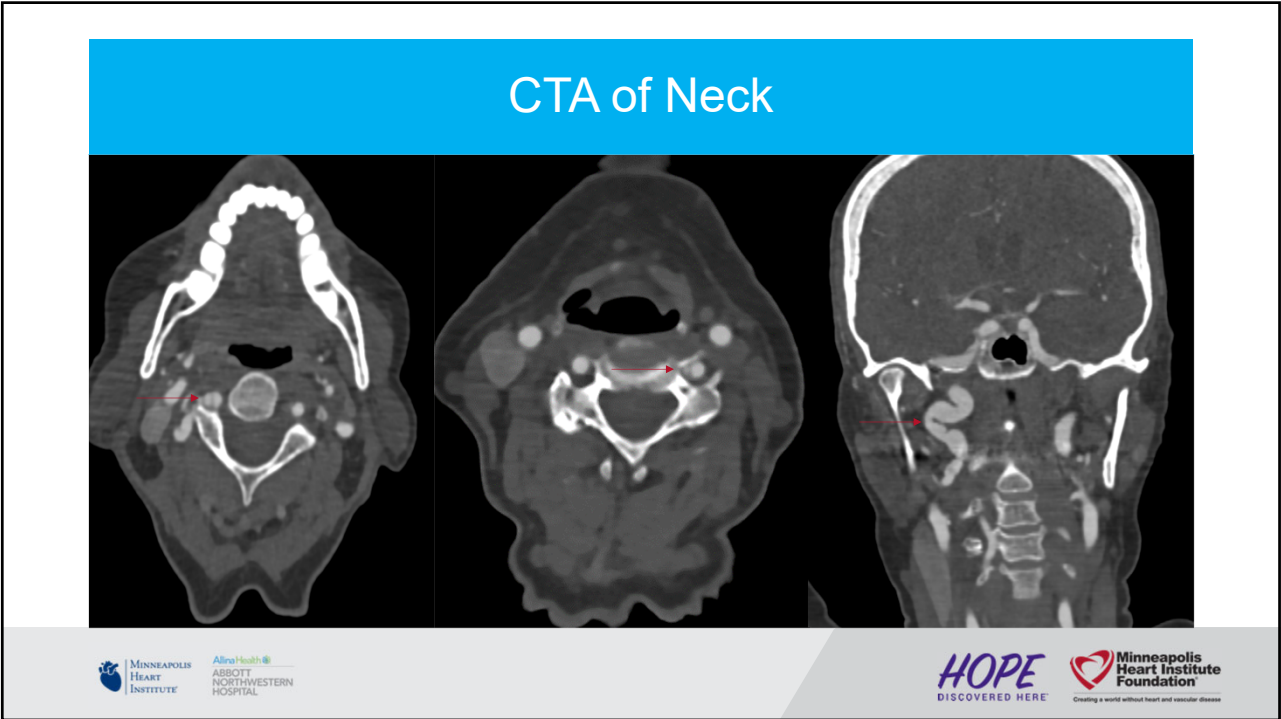
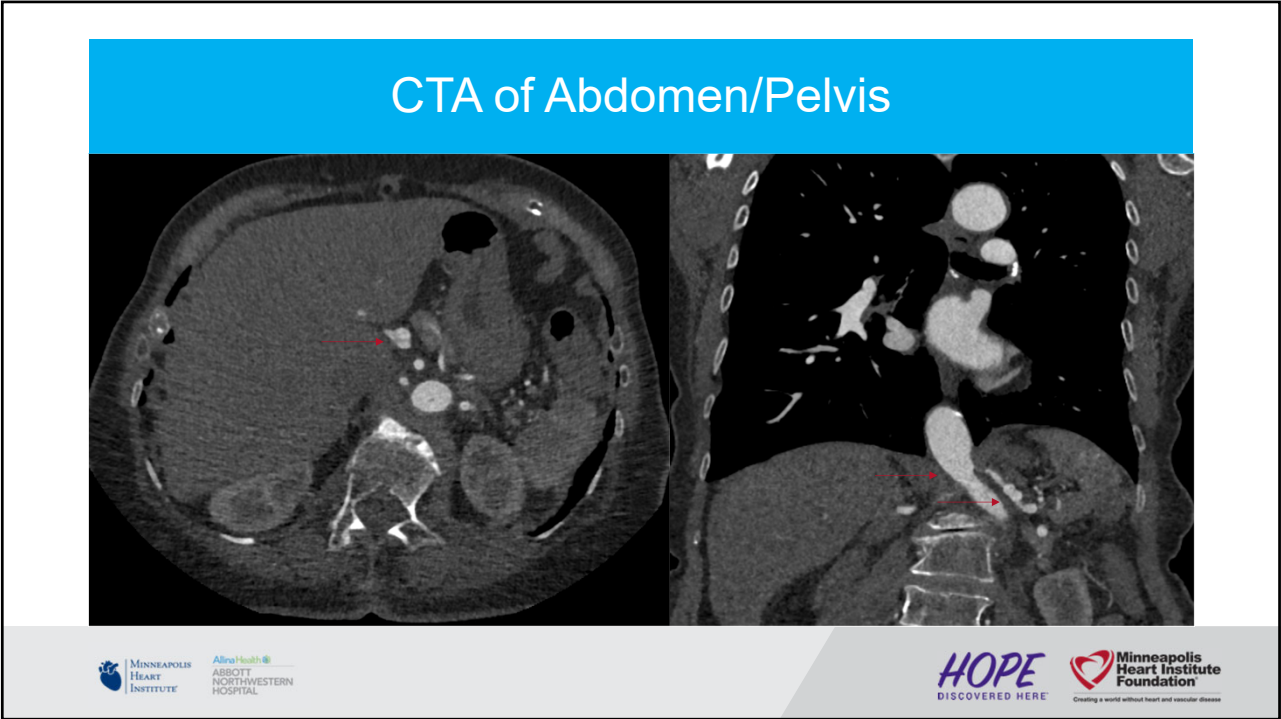
Etiologies

- Fibromuscular dysplasia (FMD)
- Segmental arterial mediolysis (SAM)
- Connective tissue disorders (vEDS, LDS, Marfan)
- Localized vasculitis of the GI tract (LGVT) or systemic vasculitis (e.g. PAN, ANCA-vasculitis)
- Median arcuate ligament syndrome (MALS)
- Trauma
- Isolated disease (dissection or aneurysm)




Case 1


- **Patient:** 74 y/o F
- **PMH:** CAD (remote history of MI) and uncontrolled HTN
- **Presentation:** abdominal and neck pain
- **Family history:** 3 sisters and one daughter with history of irregular vessels!
- **VS:** BP: 160/90 mmHg P: 80/min regular
- **Exam:** right side carotid bruit and mild epigastric tenderness
- **Labs:** ESR: 35 and CRP: 2.7




Diagnosis ?

- A- FMD
- B- SAM
- C- vEDS
- D- LDS
- E- Vasculitis







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Diagnosis: Fibromuscular Dysplasia (FMD)


- Meets criteria by *First international Consensus on the Diagnosis and Management of FMD*:
- Focal or multifocal FMD lesion (alternating stenosis and dilation) in one vascular bed +/- aneurysm, dissection, or tortuosity in another vascular bed
- Age and gender
- Beading appearance and *history of SCAD*
- No significant wall thickening or elevated ESR/CRP
- Genetic testing was negative for connective tissue disorders
- Less likely SAM: biopsy not feasible!
- Management: ASA, good BP control, and imaging surveillance.




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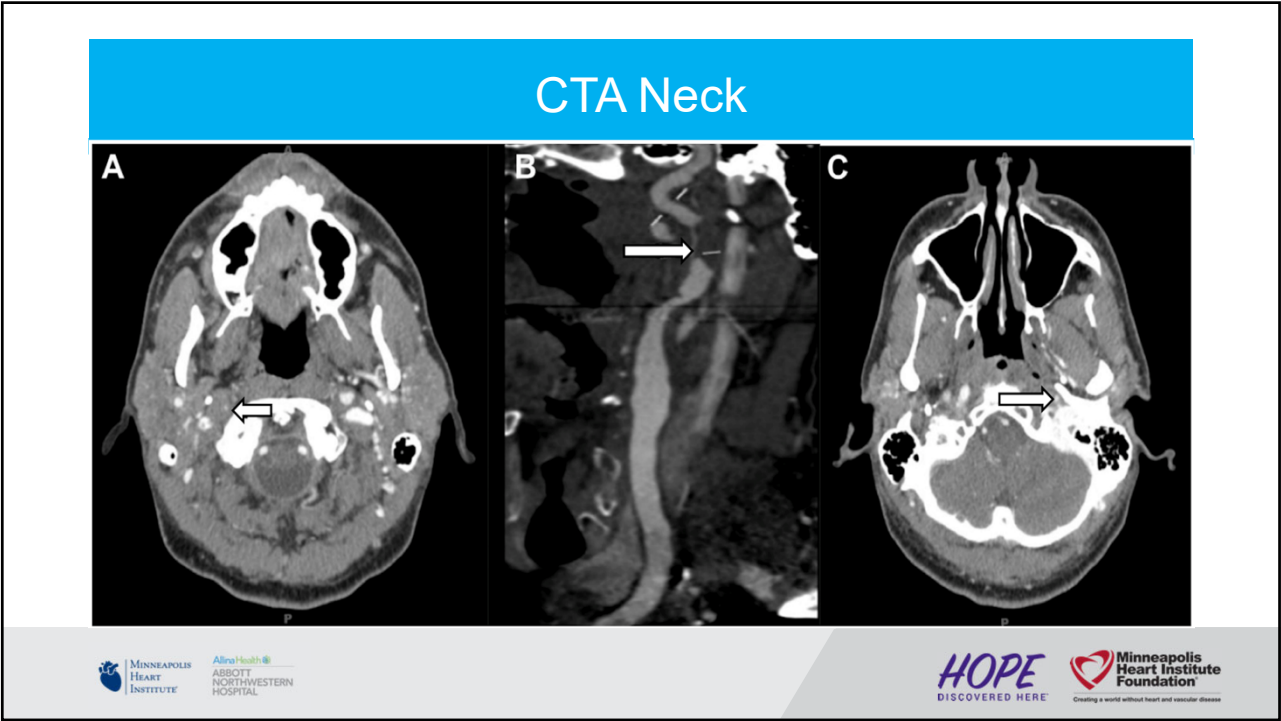
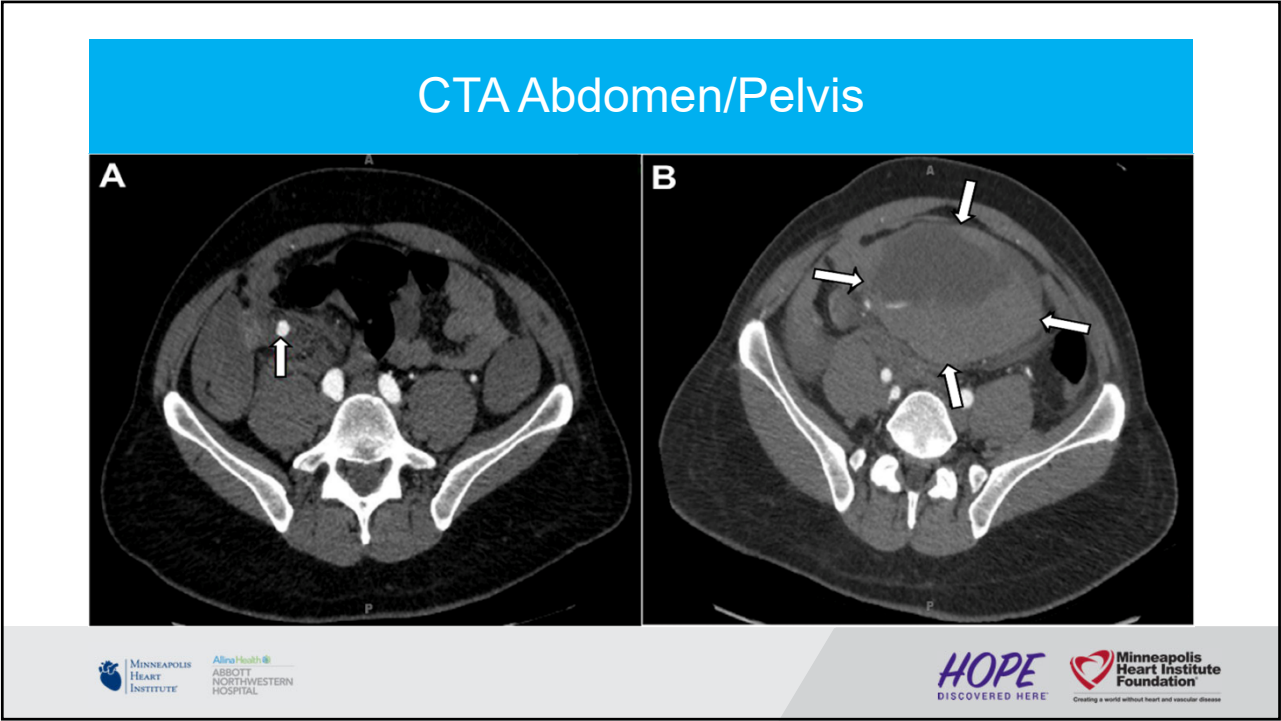
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Case 2

- **Patient:** 47 y/o M
- **PMH:** None
- **Presentation:** neck pain, headache followed by abdominal pain
- **Family history:** No relevant history
- **VS:** BP: 170/95 mmHg, P: 105/min regular
- **Exam:** Neck and diffuse abdominal tenderness
- **Labs:** ESR: 27 and CRP: 4.54

CTA of Abdomen/Pelvis





Diagnosis ?

- A- FMD
- B- SAM
- C- vEDS
- D- LDS
- E- Vasculitis



Diagnosis: Segmental Arterial Mediolysis (SAM)

- Dissection and or an aneurysm with or without organ infarction in *multiple* mesenteric and or renal arteries with *exclusion of other* vasculopathies (e.g. FMD), and no significant concurrent arterial wall thickening (< 3mm) or inflammatory markers' elevation
- Biopsy: lysis of the outer arterial media resulting in dissection and pseudoaneurysm
- Age and gender
- Dramatic presentation
- Genetic testing was negative for connective tissue disorders
- No significant wall thickening or significant ESR/CRP elevation
- Management: hematoma evacuation, blood pressure control, ASA, and imaging surveillance.

Skeik N et al. *Ann Vasc Surg*. 2017 Oct;44:422.e9-422.e13

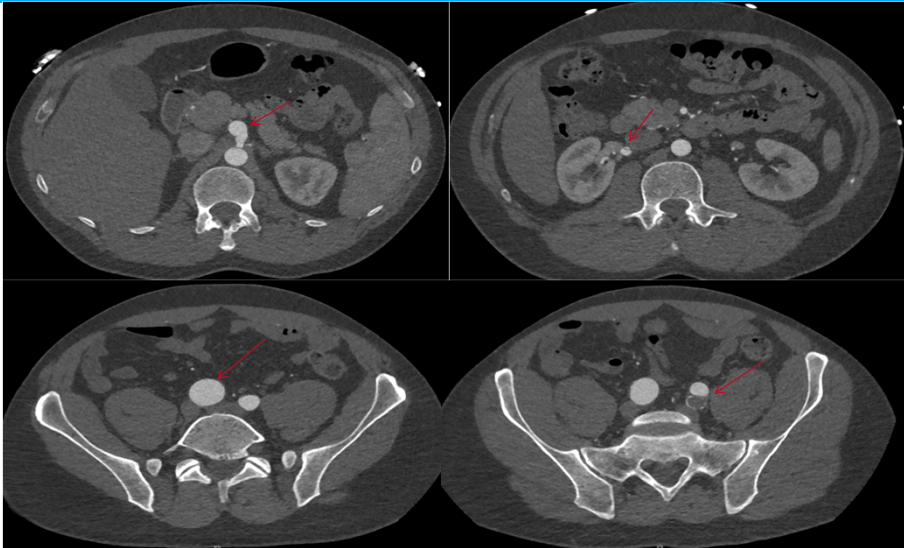


Case 3

- **Patient:** 38 y/o M
- **PMH:** Tobacco abuse
- **Family History:** Not relevant history
- **Presentation:** abdominal pain, nausea and vomiting
- **VS:** BP: 145/85 mmHg, P: 86/min regular
- **Exam:** Generalized abdominal tenderness
- **Labs:** ESR: 14 and CRP 2.23



CTA of Abdomen and Pelvis



Diagnosis ?

- A- FMD
- B- SAM
- C- vEDS
- D- LDS
- E- Vasculitis



Diagnosis: Vascular Ehler's Danlos Syndrome (vEDS)

- Genetic testing: novel frameshift variant in COL3A1
- One major criteria and positive genetic testing
- Younger patient
- Multiple arterial involvement and pathologies: aneurysms and dissection
- No significant inflammatory markers elevation
- *No suggestive family history!*
- *No connective tissue manifestations!*
- Management: ASA, BP control and imaging surveillance. Celiprolol !!

Skeik N et al. *Ann Vasc Surg*.2019 Nov;61:472.e9-472.e13

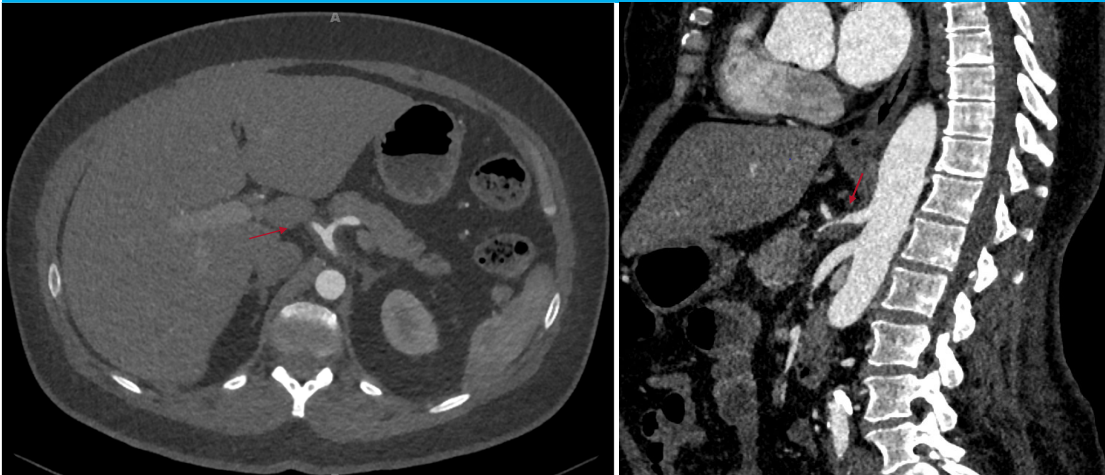


Case 4

- **Patient:** 50 y/o F
- **PMHX:** Obesity, HTN, and tobacco abuse
- **Family History:** No relevant history
- **Presentation:** Abdominal pain
- **VS:** BP: 156/87 mmHg, P: 86/min regular
- **Exam:** Severe epigastric tenderness
- **Labs:** ESR 48 and CRP: 22.67



CTA of Abdomen/Pelvis



Diagnosis ?

- A- FMD
- B- SAM
- C- vEDS
- D- LDS
- E- Vasculitis



Diagnosis: Isolated Vasculitis of the GI Tract (LVGT)

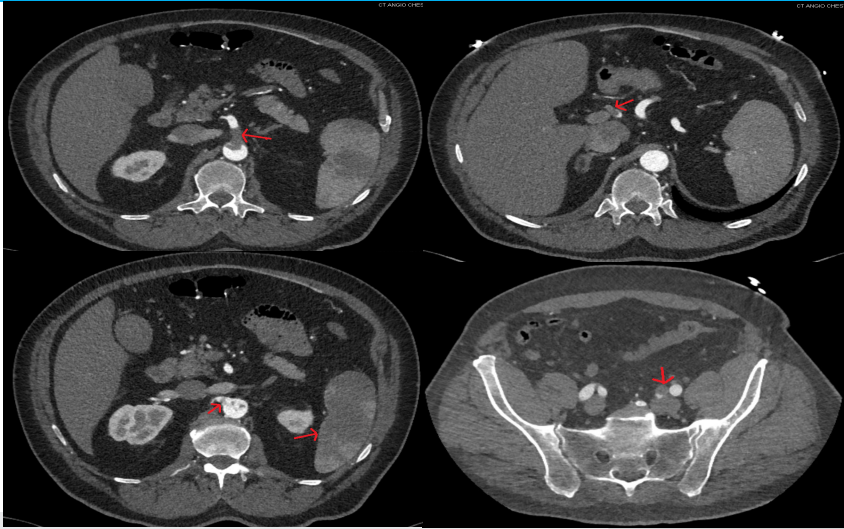
- Significant wall thickening (> 3mm) and elevated ESR/CRP
- Condition worsened within 3 weeks on ASA only
- Improved significantly on prednisone for 4 weeks
- No rheumatological symptoms
- Autoimmune work up was negative
- Negative genetic testing for connective tissue disorder
- No other arteriopathies
- Tissue biopsy was not feasible!
- Management: Prednisone taper, ASA and imaging surveillance.

Case 5

- **Patient:** 63 y/o M
- **PMH:** of AVR (St. Jude mechanical), DM, HTN, HL
- **Presentation:** Abdominal pain and nausea
- **Family history:** No relevant history
- **VS:** BP: 171/99 mmHg, P: 100/min regular
- **Exam:** mechanical S2, no murmur. Abdominal general tenderness
- **Labs:** WBC: 23,300 Hgb: 15.5, and PLT: 580,000. Over 2 years, INR levels (2.1 - 4.4)



CTA of Abdomen/Pelvis



Diagnosis ?

- A- Antiphospholipid syndrome
- B- HIT
- C- Essential thrombocythemia
- D- Malignancy
- E- Aortic Vegetation



Diagnosis: Essential Thrombocythemia

- Elevated PLT
- Positive JAK 2 mutation
- Unremarkable TEE
- Other malignancy work up was negative
- No recent heparin exposure
- Negative antiphospholipid syndrome work up
- **Management:** ASA, warfarin and hydroxyurea with resolution of the thrombi

Skeik N et al. Ann Vasc Syrg. 2017 Jul;42:306.e5-306.e10



Case 6

- **Patient:** 51 y/o F
- **PMHX:** none
- **Presentation:** Postprandial epigastric abdominal pain with nausea and weight loss (20 pounds in 1 year)
- **Family history:** No relevant history
- **VS:** Normal
- **Exam:** Epigastric tenderness with epigastric bruit with expiration
- **Labs:** CBC, CMP, LFT's, lipase were normal

CTA of Abdomen/Pelvis



Diagnosis ?

- A- FMD
- B- SAM
- C- vEDS
- D- Median Arcuate Ligament Syndrome (MALS)
- E- Vasculitis



Diagnosis: Median Arcuate Ligament Syndrome

- Typical symptoms and images
- No other explanation
- Negative work up: EGD, colonoscopy, celiac, depression, ..
- Management:
 - Ganglion block: good response
 - Median arcuate ligament release
 - ASA


Skeik N et al. *Vasc Endovascular Surg.* 2011 Jul;45(5):433-7



Differential Diagnoses!







Non-atherosclerotic Abdominal Vasculopathies

*Single Center Retrospective Analysis of Patients:(Age: 18-60)
Presented with NAV Between 01/2000 and 12/2015*



• **Pathologies:**

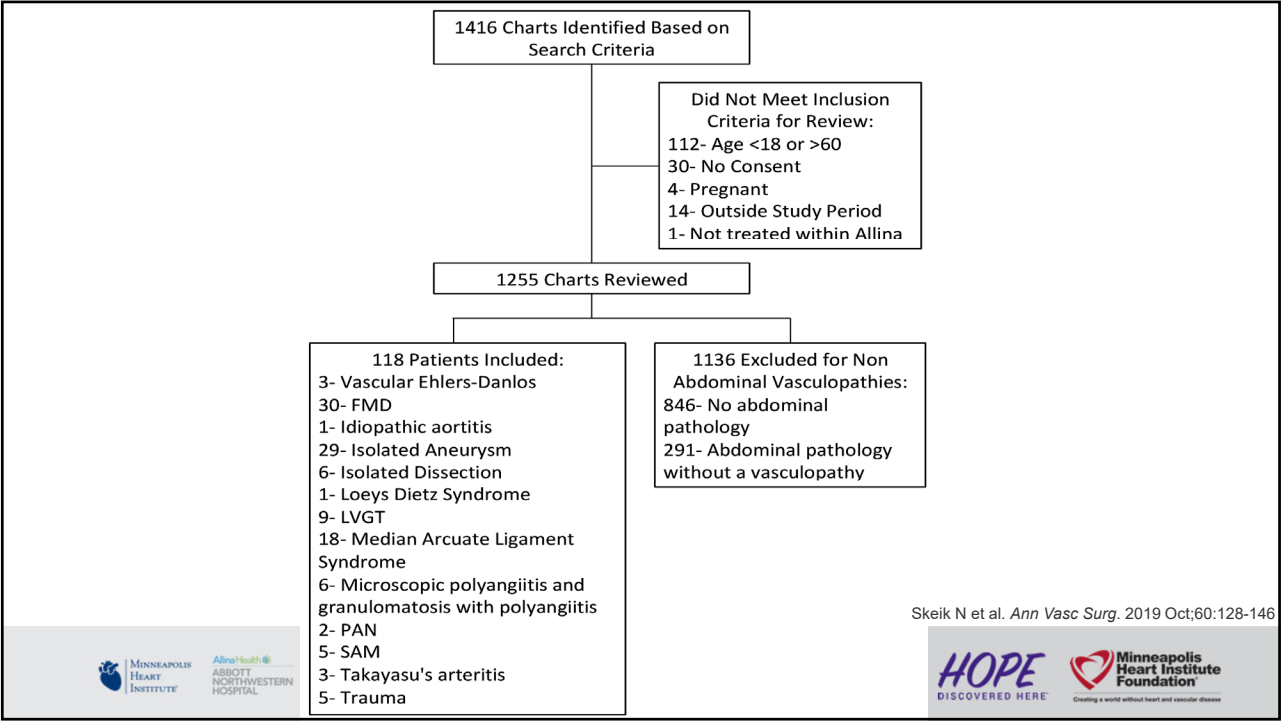
- Arterial stenosis
- Wall thickening
- Dissection
- Aneurysm
- Pseudoaneurysm

• **Arterial Involvement:**

- Renal
- Celiac
- Hepatic
- Splenic
- Mesenteric arteries

Skeik N et al. *Ann Vasc Surg*. 2019 Oct;60:128-146





Data Collection

- **Demographics:** date of birth, gender
- **Comorbid Conditions:** DM, HTN, HL, current or history of tobacco use, PAD, and CAD
- **Presenting symptoms**
- **Physical Exam**
- **Medications**
- **Laboratory data and diagnostic imaging:** at initial presentation and at follow-up visits

Skeik N et al. *Ann Vasc Surg.* 2019 Oct;60:128-146

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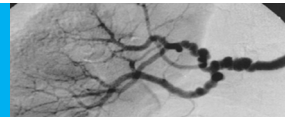
Diagnoses

- Most commonly used diagnostic criteria..
- Consensus guidelines
- Societies (SVM, SVS..)
- Expert opinion
- Some diagnoses were presumed (no pathology or genetic testing)

Skeik N et al. *Ann Vasc Surg.* 2019 Oct;60:128-146



Fibromuscular Dysplasia (FMD)

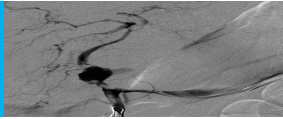


- Non-atherosclerotic arterial disease with abnormal cellular proliferation and wall architecture.
- Primarily manifests as beaded (multifocal) or focal lesions in medium or small-sized arteries.
- Phenotype now expanded to include arterial dissection, aneurysm, and tortuosity.
- Most commonly affects the renal and extracranial carotid and vertebral arteries, but nearly all arterial beds may be affected, and multi-vessel involvement is common.
- 90% female predominance!
- **Diagnostic Criteria:**
 - Stenosis, occlusion, dissection, or aneurysm in the renal and/or extracranial cerebrovascular arteries with concurrent string of beading appearance (multifocal FMD) or circumferential stenosis (focal FMD) in the setting of no aortic involvement and no significant inflammatory markers' elevation.

Skeik N et al. *Ann Vasc Surg.* 2019 Oct;60:128-146



Segmental Arterial Mediolyis (SAM)

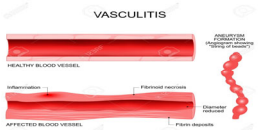


- Rare but serious non-atherosclerotic, noninflammatory vasculopathy of unknown etiology.
- Characterized by vacuolar degeneration and lysis of the medial layer, often resulting in dissection, aneurysm, occlusion, or stenosis.
- Commonly affects the abdominal aortic branches, such as the celiac, mesenteric, and/or renal arteries with occasional carotid, cerebral, and coronary artery involvement.
- Slightly more common in males!
- **Diagnostic Criteria:**
 - Dissection and or an aneurysm with or without organ infarction in *multiple* mesenteric and or renal arteries with exclusion of connective tissue disorders, FMD, or other vasculopathies, and no significant concurrent arterial wall thickening (< 3mm) or inflammatory markers' elevation.

Skeik N et al. *Ann Vasc Surg.* 2019 Oct;60:128-146



Localized Vasculitis of the GI Tract (LVGIT)



- Single organ vasculitis of the GI tract.
- Imaging: wall thickening +/- stenosis, occlusion or aneurysm of GI arteries.
- Diagnosis: symptoms + images +/- path. Always presumptive and requires exclusion of systemic illness at the time of diagnosis and over a 6-month follow-up period.
- **Diagnostic Criteria:**
 - Acquired GI manifestations (including abdominal pain, nausea or vomiting, diarrhea, weight loss, melena) and a histopathological evidence of vasculitis in a GI specimen; or high-probability angiographic findings (smooth segmental narrowing, dilatation, occlusion or aneurysms affecting one or more GI arteries) with significant wall thickening ($\geq 3\text{mm}$) and the absence of vessel changes consistent with atherosclerosis, FMD or SAM).
 - Inflammatory markers can be normal or elevated!

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Vascular Ehlers-Danlos Syndrome (vEDS)



- Life-threatening arteriopathy caused by genetic alteration of COL3A1 gene.
- *Major criteria:* arterial rupture, intestinal rupture, uterine rupture or positive family history.
- *Minor criteria:* thin translucent skin, characteristic facial appearance (thin face, large appearing eyes, thin lips and nose), acrogeria, hypermobility of small joints, tendon and muscle rupture, talipes equinovarus, early onset varicosities, pneumothorax, gingival recession.
- *Two major criteria* are considered highly specific.
- *Two minor criteria* requires further testing to confirm the diagnosis of EDS.
- *Genetic testing:* sequence and deletion/duplication testing of the COL3A1 gene.
- **Diagnostic Criteria:**
 - Positive Villefranche criteria and genetic testing (COL3A1 gene).

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Loeys-Dietz Syndrome (LDS)

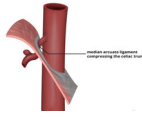


- Autosomal dominant syndrome with aortic-aneurysm and systemic involvement (cardiovascular, craniofacial, skeletal, neurocognitive, and cutaneous malformations).
- *Diagnosis consideration:* hypertelorism, a bifid uvula and/or cleft palate and generalized arterial tortuosity with widespread vascular aneurysm and dissection.
- *Diagnosis confirmation:* genetic alteration in 5 genes: transforming growth factor beta receptors 1 or 2, SMAD family member 3, or transforming growth factor beta 2 or 3, resulting in 5 LDS subtypes with less functional protein.
- *LDS type 3* (mutations of SMAD3): characterized more specifically by aortic and arterial aneurysms and dissections.
- **Diagnostic Criteria:**
 - Phenotype and genotype consistent with LDS

Skeik N et al. *Ann Vasc Surg.* 2019 Oct;60:128-146



Median Arcuate Ligament Syndrome (MALS)



- Celiac artery compression by median accurate ligament
- Arterial and neurogenic syndrome
- Diagnosis of exclusion
- **Diagnostic Criteria:**
 - Combination of symptoms (e.g. postprandial abdominal pain, weight loss), typical CTA findings of celiac artery compression by the median arcuate ligament with post-stenotic dilation or aneurysm, and increased velocity during exhalation compared with inhalation in an ultrasound.

Skeik N et al. *Ann Vasc Surg*. 2019 Oct;60:128-146



Demographics and Comorbidities

	All Patients (n=118)	FMD (n=30)	Isolated aneurysm (n=29)	MALS (n=18)	LVGT (n=9)	Isolated Dissection (n=6)	MP/GP (n=6)	Trauma (n=5)	SAM (n=5)	EDS (n=3)	Takayasu's Arteritis (n=3)	PAN (n=2)	LDS (n=1)
Age (Year)	50.5 (39.0, 54.0)	50 (43, 54)	52 (39, 54)	50 (38, 51)	51 (41, 55)	45.5 (35, 54)	56 (54, 59)	50 (42, 59)	54 (52, 55)	41 (24, 53)	35 (26, 36)	51 (43, 59)	34
Male, (%)	42 (35.6)	3 (10.0)	7 (24.1)	4 (22.2)	4 (44.4)	6 (100)	4 (66.7)	5 (100)	5 (100)	3 (100)	1 (33.3)	0 (0)	0 (0)
Hypertension, (%)	61 (52.1)	18 (60.0)	12 (41.4)	6 (33.3)	4 (44.4)	3 (50.0)	2 (40.0)	4 (80.0)	5 (100)	2 (66.7)	2 (66.7)	2 (100)	1 (100)
Tobacco Use, (%)	51 (43.6)	16 (53.3)	10 (35.7)	6 (33.3)	5 (55.6)	3 (50.0)	2 (33.3)	3 (60.0)	3 (60.0)	1 (33.3)	1 (33.3)	0 (0)	1 (100)
Hyperlipidemia, (%)	20 (17.1)	6 (20.0)	5 (17.2)	0 (0)	2 (22.2)	2 (33.3)	1 (20.0)	0 (0)	2 (40.0)	0 (0)	1 (33.3)	1 (50.0)	0 (0)
Diabetes, (%)	10 (8.6)	4 (13.3)	4 (13.8)	0 (0)	0 (0)	0 (0)	1 (20.0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (50.0)	0 (0)
CAD, (%)	10 (8.6)	2 (6.7)	3 (10.3)	0 (0)	1 (11.1)	1 (16.7)	0 (0)	0 (0)	1 (20.0)	0 (0)	1 (33.3)	1 (50.0)	0 (0)
PAD, (%)	6 (5.1)	3 (10.0)	0 (0)	1 (5.6)	0 (0)	0 (0)	0 (0)	0 (0)	1 (20.0)	0 (0)	1 (33.3)	0 (0)	0 (0)

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Arterial Pathology

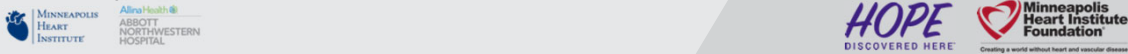
	All Patients (n=118)	FMD (n=30)	Isolated aneurysm (n=29)	MALS (n=18)	LVGT (n=9)	Isolated Dissection (n=6)	MP/GP (n=6)	Trauma (n=5)	SAM (n=5)	EDS (n=3)	Takayasu's Arteritis (n=3)	PAN (n=2)	LDS (n=1)
Aneurysm	70 (59.3)	24 (80.0)	29 (100)	3 (16.7)	1 (11.1)	0 (0)	0 (0)	4 (80)	5 (100)	2 (66.7)	0 (0)	1 (50.0)	1 (100)
Stenosis	48 (40.7)	11 (36.7)	1 (3.5)	18 (100)	9 (100)	1 (16.7)	0 (0)	0 (0)	4 (80.0)	0 (0)	3 (100)	0 (0)	0 (0)
Dissection	29 (24.6)	9 (30.0)	0 (0)	1 (5.6)	3 (33.3)	6 (100)	0 (0)	4 (80)	3 (60.0)	2 (66.7)	0 (0)	0 (0)	1 (100)
Thrombosis	29 (24.6)	7 (23.3)	6 (20.7)	1 (5.6)	2 (22.2)	5 (83.3)	0 (0)	1 (20)	3 (60.0)	2 (66.7)	1 (33.3)	0 (0)	0 (0)
Renal Infarction	13 (11.0)	6 (20.0)	0 (0)	0 (0)	1 (11.1)	4 (66.7)	0 (0)	0 (0)	1 (20.0)	1 (33.3)	0 (0)	0 (0)	0 (0)

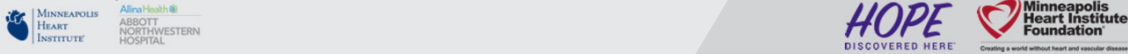
Skeik N et al. *Ann Vasc Surg.* 2019 Oct;60:128-146

Arterial Involvement

	All Patients (n=118)	FMD (n=30)	Isolated aneurysm (n=29)	MALS (n=18)	LVGT (n=9)	Isolated Dissection (n=6)	MP/GP (n=6)	Trauma (n=5)	SAM (n=5)	EDS (n=3)	Takayasu's Arteritis (n=3)	PAN (n=2)	LDS (n=1)
Renal Artery	52 (44.1)	25 (83.3)	7 (24.1)	1 (5.6)	1 (11.1)	5 (83.3)	6 (100)	1 (20)	2 (40.0)	2 (66.7)	2 (66.7)	1 (50.0)	0 (0)
Right	16 (30.9)	9 (36.0)	4 (57.1)	0 (0)	0 (0)	0 (0)	0 (0)	1 (100)	0 (0)	0 (0)	2 (66.7)	0 (0)	0 (0)
Left	15 (28.9)	5 (20.0)	3 (42.9)	1 (100)	1 (100)	4 (80.0)	0 (0)	0 (0)	0 (0)	1 (50.0)	0 (0)	0 (0)	0 (0)
Bilateral	22 (40.4)	11 (44.0)	0 (0)	0 (0)	0 (0)	1 (20.0)	6 (100)	0 (0)	2 (100)	1 (50.0)	0 (0)	1 (100)	0 (0)
Celiac artery	43 (36.4)	7 (23.3)	3 (10.3)	18 (100)	4 (44.4)	0 (0)	0 (0)	3 (60.0)	5 (100)	2 (66.7)	1 (33.3)	0 (0)	0 (0)
Splenic artery	31 (26.3)	9 (30.0)	17 (58.6)	0 (0)	2 (22.2)	0 (0)	0 (0)	1 (20.0)	1 (20.0)	0 (0)	0 (0)	1 (50.0)	0 (0)
SMA	23 (19.5)	3 (10.0)	2 (6.9)	2 (11.1)	5 (55.6)	1 (16.7)	0 (0)	3 (60.0)	3 (60.0)	0 (0)	2 (66.7)	1 (50.0)	1 (100)
Hepatic artery	8 (6.8)	2 (6.7)	0 (0)	0 (0)	1 (11.1)	0 (0)	0 (0)	0 (0)	2 (40.0)	1 (33.3)	1 (33.3)	0 (0)	1 (100)
IMA	4 (3.4)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (20.0)	0 (0)	1 (33.3)	1 (50.0)	0 (0)

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Vital Signs and Laboratory Findings													
	All Patients (n=118)	FMD (n=30)	Isolated aneurysm (n=29)	MALS (n=18)	LVGT (n=9)	Isolated Dissection (n=6)	MP/GP (n=6)	Trauma (n=5)	SAM (n=5)	EDS (n=3)	Takayasu's Arteritis (n=3)	PAN (n=2)	LDS (n=1)
SBP	122 (110, 135) (n=95)	129 (120, 137) (n=24)	116.5 (110, 124.5) (n=24)	114 (105, 124) (n=16)	134 (120, 145) (n=9)	135 (115.5, 156.5) (n=4)	130 (116, 140) (n=3)	130 (124, 147.5) (n=4)	124 (124, 124) (n=1)	146 (120, 152) (n=3)	110 (108, 146) (n=3)	110 (n=1)	102 (n=1)
DBP	76 (66, 86) (n=95)	81 (70, 90.5) (n=24)	72 (65, 80) (n=24)	71 (65, 83) (n=16)	79 (74, 89) (n=9)	79.5 (69.5, 96) (n=4)	68 (60, 71) (n=3)	80 (75, 91.5) (n=4)	78 (78, 78) (n=1)	94 (64, 100) (n=3)	62 (60, 86) (n=3)	60 (n=1)	56 (n=1)
Hemoglobin	13.3 (12.1, 14.6) (n=88)	13.1 (11.9, 14.5) (n=22)	13.1 (12.4, 14) (n=20)	14.05 (12.1, 14.7) (n=14)	14 (13.8, 15.3) (n=9)	14.6 (13.8, 16) (n=5)	11.1 (10.6, 12.3) (n=4)	14.7 (12.1, 15.6) (n=3)	11.9 (9.2, 14.2) (n=3)	13.15 (13, 13.3) (n=2)	11.15 (9.1, 13.2) (n=2)	12.45 (12.2, 12.7) (n=2)	7.1 (n=1)
ESR	23 (16, 51) (n=39)	27 (15, 45) (n=5)	51 (14, 75) (n=7)	19 (16, 22) (n=3)	23 (22, 42) (n=9)	34 (20, 44) (n=3)	54 (22, 74) (n=4)	-----	18 (16, 70) (n=3)	10 (n=1)	33 (14, 54) (n=3)	-----	44 (n=1)
Elevated ESR, (%)	21/39 (53.9)	3 (60.0)	4 (57.1)	0 (0)	4 (44.4)	3 (100)	3 (75.0)	-----	2 (66.7)	0 (0)	2 (66.7)	-----	1 (100)
CRP	1.2 (0.5, 3.5) (n=33)	0.65 (0.5, 6.8) (n=8)	3.35 (1.85, 5.85) (n=4)	0.9 (0.5, 1.3) (n=2)	2 (0.6, 2.94) (n=9)	13.25 (6.9, 19.6) (n=2)	1.2 (0.6, 1.8) (n=2)	11.8 (n=1)	3.1 (2.6, 3.6) (n=2)	0.5 (n=1)	0.5 (n=1)	-----	0.7 (n=1)
Elevated CRP, (%)	31/33 (93.9)	7 (87.5)	4 (100)	2 (100)	8 (88.9)	2 (100)	2 (100)	1 (100)	2 (100)	1 (100)	1 (100)	-----	1 (100)
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Type of Imaging													
Type of Imaging	All Patients (n=118)	FMD (n=30)	Isolated aneurysm (n=29)	MALS (n=18)	LVGT (n=9)	Isolated Dissection (n=6)	MP/GP (n=6)	Trauma (n=5)	SAM (n=5)	EDS (n=3)	Takayasu's Arteritis (n=3)	PAN (n=2)	LDS (n=1)
CTA/CT	99 (83.9)	24 (80.0)	28 (96.6)	14 (77.8)	9 (100)	6 (100)	1 (16.7)	5 (100)	5 (100)	3 (100)	1 (33.3)	1 (50.0)	1 (100)
MRA	21 (18.0)	9 (30.0)	1 (3.5)	4 (22.2)	2 (22.2)	0 (0)	0 (0)	0 (0)	1 (20.0)	2 (66.7)	2 (66.7)	0 (0)	0 (0)
DUS/US	15 (12.7)	3 (10.0)	0 (0)	5 (27.8)	0 (0)	2 (33.3)	1 (16.7)	2 (20.0)	1 (20.0)	1 (33.3)	0 (0)	0 (0)	0 (0)
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Presenting Findings and Symptoms

	All Patients (n=118)	FMD (n=30)	Isolated aneurysm (n=29)	MALS (n=18)	LVGT (n=9)	Isolated Dissection (n=6)	MP/GP (n=6)	Trauma (n=5)	SAM (n=5)	EDS (n=3)	Takayasu's Arteritis (n=3)	PAN (n=2)	LDS (n=1)
Abdominal/Flank Pain	65 (55.1)	14 (46.7)	8 (27.6)	13 (72.2)	9 (100)	6 (100)	1 (16.7)	5 (100)	4 (80.0)	2 (66.7)	1 (33.3)	1 (50.0)	0 (0)
Nausea/Vomiting	17 (14.4)	3 (10.0)	2 (6.9)	6 (33.3)	3 (33.3)	1 (16.7)	1 (16.7)	0 (0)	0 (0)	1 (33.3)	0 (0)	0 (0)	0 (0)
Diarrhea	8 (6.8)	2 (6.7)	0 (0)	4 (22.2)	0 (0)	1 (16.7)	0 (0)	1 (20.0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Asymptomatic	31 (26.3)	3 (10.0)	21 (72.4)	3 (16.7)	0 (0)	0 (0)	0 (0)	0 (0)	1 (20.0)	1 (33.3)	1 (33.3)	0 (0)	1 (100)

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Management



	All Patients (n=118)	FMD (n=30)	Isolated aneurysm (n=29)	MALS (n=18)	LVGT (n=9)	Isolated Dissection (n=6)	MP/GP (n=6)	Trauma (n=5)	SAM (n=5)	EDS (n=3)	Takayasu's Arteritis (n=3)	PAN (n=2)	LDS (n=1)
Coil Embolization	17 (14.4)	6 (20.0)	7 (24.1)	1 (5.6)	1 (10.0)	0 (0)	0 (0)	0 (0)	1 (20.0)	0 (0)	0 (0)	1 (50.0)	0 (0)
Angioplasty/Stenting	14 (11.9)	5 (16.7)	1 (3.5)	3 (16.7)	0 (0)	2 (33.3)	0 (0)	1 (20.0)	0 (0)	1 (33.3)	1 (33.3)	0 (0)	0 (0)
Anticoagulation	14 (11.9)	5 (16.7)	0 (0)	1 (5.6)	2 (22.2)	1 (16.7)	0 (0)	1 (20.0)	3 (60.0)	1 (33.3)	0 (0)	0 (0)	0 (0)
Open Resection/Surgical Revascularization	12 (10.2)	4 (13.3)	4 (13.8)	3 (16.7)	0 (0)	0 (0)	0 (0)	1 (20.0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Prednisone	12 (10.2)	0 (0)	0 (0)	0 (0)	4 (44.4)	0 (0)	6 (100)	0 (0)	1 (20.0)	0 (0)	2 (66.7)	1 (50.0)	0 (0)
Splenectomy	6 (5.1)	2 (6.7)	4 (13.8)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Open MALS release	4 (3.4)	0 (0)	0 (0)	4 (22.2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Laparoscopic MALS release	3 (2.6)	0 (0)	0 (0)	3 (16.7)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Nephrectomy	1 (0.9)	1 (3.33)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Conservative treatment	39 (33.1)	9 (30.0)	16 (55.2)	4 (22.2)	2 (22.2)	3 (50.0)	0 (0)	2 (40.0)	1 (20.0)	1 (33.3)	0 (0)	0 (0)	1 (100)







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Outcomes													
	All Patients	FMD	Isolated aneurysm	MALS	LVGT	Isolated Dissection	MP/GP	Trauma	SAM	EDS	Takayasu's Arteritis	PAN	LDS
	(n=118)	(n=30)	(n=29)	(n=18)	(n=9)	(n=6)	(n=6)	(n=5)	(n=5)	(n=3)	(n=3)	(n=2)	(n=1)
Symptoms relieved	77/84 (91.7)	20/21 (95.2)	13/14 (92.9)	10/14 (71.4)	7/8 (87.5)	5 (100)	6 (100)	5 (100)	4 (100)	2 (100)	2 (100)	1 (100)	1 (100)
Symptoms recurred	12/83 (14.5)	3/21 (14.3)	2/13 (15.4)	3/14 (21.4)	1/2 (12.5)	0 (0)	2 (33.3)	1 (20)	0 (0)	0 (0)	0/2 (0)	0/1 (0)	0 (0)
Surgical Success	32/86 (27.1)	13 (43.3)	8 (27.6)	4 (22.2)	1 (11.1)	1 (16.7)	0 (0)	2 (40.0)	1 (20.0)	1 (33.3)	1 (33.3)	0 (0)	0 (0)
Imaging													
Improved, (%)	17 (30.4)	8 (36.4)	0 (0)	0 (0)	4 (44.4)	3 (60.0)	0 (0)	1 (20.0)	0 (0)	1 (33.3)	0 (0)	0 (0)	0 (0)
Unchanged, (%)	16 (28.6)	9 (40.9)	1 (33.3)	0 (0)	0 (0)	0 (0)	1 (100)	2 (40.0)	0 (0)	1 (33.3)	2 (66.7)	0 (0)	0 (0)
Worse, (%)	4 (7.1)	2 (9.1)	1 (33.3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (33.3)	0 (0)	0 (0)	0 (0)	0 (0)
No F/U Done, (%)	19 (33.9)	3 (13.6)	1 (33.3)	0 (0)	5 (55.6)	2 (40.0)	0 (0)	2 (40.0)	2 (66.7)	1 (33.3)	1 (33.3)	0 (0)	1 (100)



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Summary	
	Demographics: 118 study participants, Age: 47.0 ± 9.9 years, Female: (64.4%)
	Comorbidities: HTN (52.1%) and tobacco use (43.6%)
	Diagnoses: FMD (25.4%), isolated aneurysms (24.6%), MALS (15.3%), LVGT (7.6%), isolated dissection (5.1%), MP/GP (5.1%), trauma (4.2%), SAM (4.2%), Takayasu's arteritis (2.5%), EDS (2.5%), PAN (1.7%), and LDS (0.8%).
	Pathologies: Aneurysms (59.3%), stenosis (40.7%), dissection (24.6%), and thrombosis in 24.6%.
	Arterial Involvement: renal (44.1%), celiac (36.4%), and splenic (26.3%).
	Images: CT (83.9 %), CBA (19.7%), MRA (18.0%), and duplex ultrasound (12.7%).

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Summary II



Labs: ESR and CRP diagnostic role is ???!!

Genetic Testing +/- Pathology: multiple arterial involvement+ beading: SAM vs. FMD vs. vEDS



Symptoms: abdominal pain (55.1%), nausea and vomiting (14.4%), diarrhea (6.8%) and (37.3%) were asymptomatic.



Management: Coil embolization (14.4%), angioplasty/stenting (11.9%), anticoagulation (11.9%), open resection/surgical revascularization (10.2%), prednisone (10.2%) and conservative treatment (33.1%).



Outcome: During a median follow-up time of 686 days the majority (91.7%) of patients had relief of their symptoms. Of the 37 pts who had f/u imaging, 30.4% showed improvement, 28.6% remained unchanged, and 7.1% worsened.

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Segmental Arterial Mediolytic Systemic Review & Data Analysis of 143 Patients

- Literature review of all relevant SAM case studies from 2005 to 2018 yielded 126 individual SAM cases from 66 reports.
- Included papers: reported patient demographics (at least age and gender), arterial involvement, arteriopathy, and diagnostic strategy (imaging or labs or histology or symptoms).
- We identified 17 additional SAM cases from our center, bringing our analysis to 143 patients.



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SAM Diagnosis

- Our Diagnostic Criteria:**
 - Dissection and/or aneurysm with or without organ infarction in *multiple* mesenteric and/or renal arteries with exclusion of FMD, LVGT, connective tissue disorder, or other vasculopathies, and no significant concurrent arterial wall thickening (< 3 mm) or elevation of inflammatory markers (erythrocyte sedimentation rate (ESR) < 20 mm/h and C-reactive protein (CRP) < 5 mg/dL)
- Different authors used different diagnostic criteria!
- **Tissue diagnosis if possible:** Vacuolar degeneration and lysis of the medial layer of the arterial wall, often resulting in dissection, aneurysm, occlusion, or stenosis
- **Differential Diagnoses:** same process as the previous project

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Demographics

Variable	
Age (year)	55 (48, 63)
Male	67.8 %
Hypertension	42.7 %
History of Tobacco Use	11.9 %
Hyperlipidemia	11.9 %
Diabetes	1.4 %





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Presenting Symptoms	
Presentation	%
Abdominal/Flank Pain	79.7
Intra-abdominal bleeding	49.7
Nausea/Vomiting	16.1
Cerebrovascular symptoms	11.9
Melena/Hematochezia	5.6
Asymptomatic	4.9
Diarrhea	4.9
Shock	4.2

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Vital Signs and Labs	
Vital Signs and Labs	%
Hypertension	42.4
Hypotension	25.4
Low Hemoglobin	50.8
Low Hematocrit	46.7
Elevated ESR	33.3
Elevated CRP	68.6

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Diagnostic Imaging	
Modality	%
CT/CTA	77.6
CBA	35
Laparotomy	32.9
MRA	9.1
US/DUS	9.1
Other	9.8

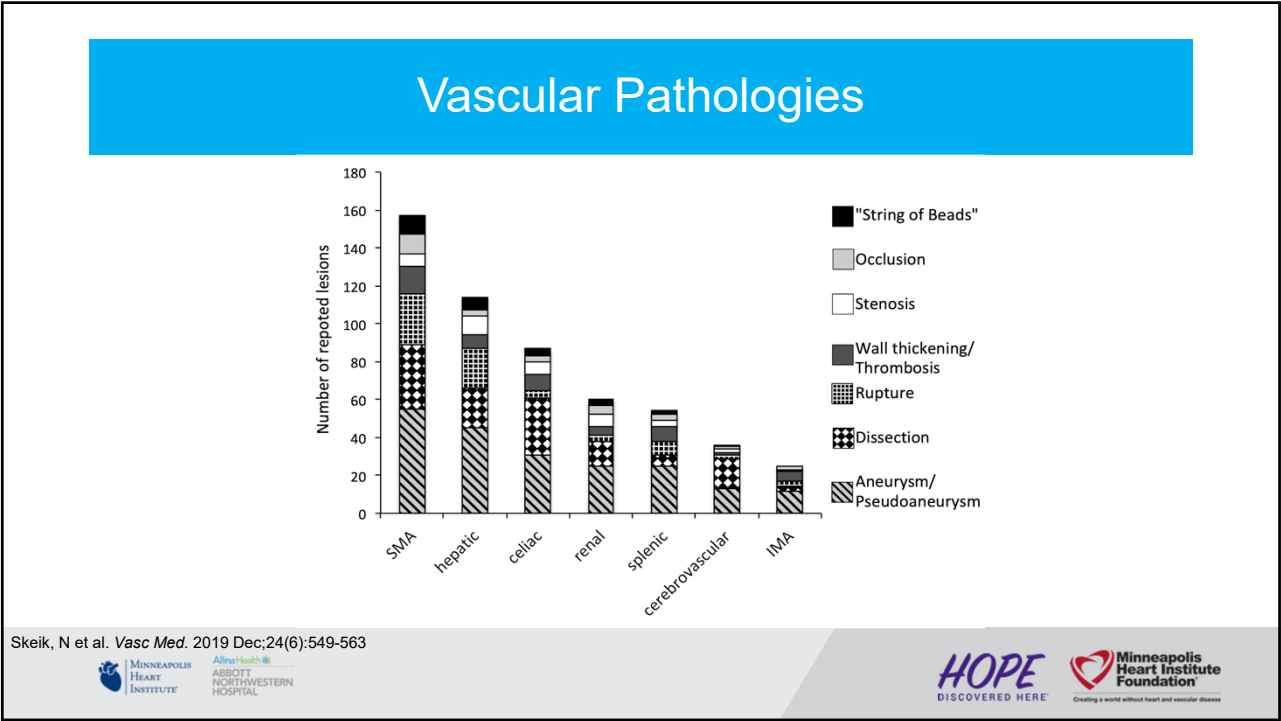
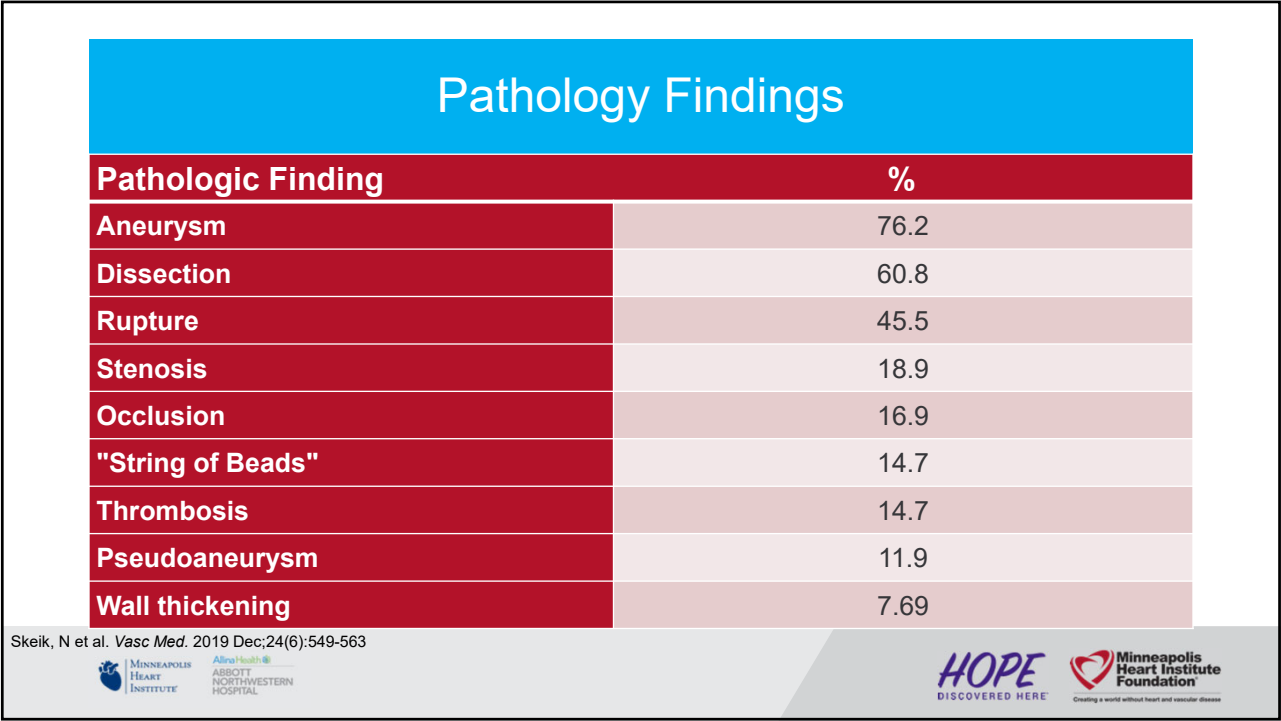
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Arterial Involvement	
Arterial Involvement	%
SMA	53.1
Hepatic	44.8
Celiac	35.7
Renal	25.9
Splenic	24.5
Cerebrovascular	13.3
IMA	10.5
Multiple	62.2



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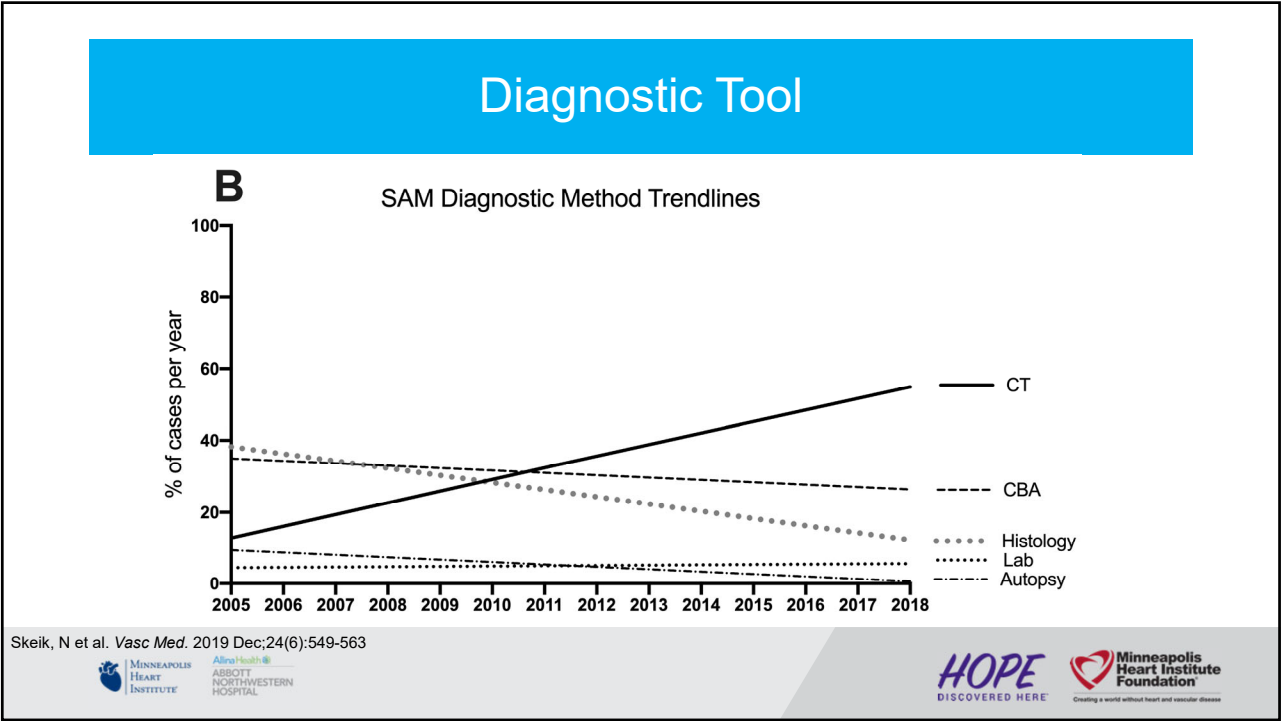


Diagnostic Criteria	
Diagnostic Tool	%
CT/CTA	59.4
Histology	44.1
CBA	29.4
Labs	10.5
Autopsy	5.6

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Management	
Modality	%
Coil Embolization	27.9
Abdominal organ surgery	23.5
Open artery repair	20.6
Antihypertensives	19.9
Anticoagulation	11.8
Antiplatelets	10.3
Angioplasty/Stenting	8.1
Conservative treatment	8.1

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Outcomes	
Outcomes	%
Survived	93
Symptoms reported	70.6
Improved	90.6
Unchanged	5.2
Worsened	4.2
Imaging	58.8
Improved	66.3
Unchanged	17.5
Worsened	16.3
No F/U Reported	28.7



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Segmental Arterial Mediolyis (SAM) vs. Fibromuscular Dysplasia (FMD)		
Demographics	SAM	FMD
Age at onset	50-60s	40-50s
Gender	67% Male	80-90% Female
History	Usually spontaneous	Drug-resistant hypertension, abdominal bruit, some cases with family history
Presentation	More dramatic and severe: Abdominal pain, intra-abdominal bleeding	Less severe: Asymptomatic, hypertension, abdominal pain, headaches



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Segmental Arterial Mediolyis (SAM) vs. Fibromuscular Dysplasia (FMD)		
Arteries involved	SAM	FMD
SMA	53%	Mesenteric 22%
Hepatic	45%	
Celiac	36%	
Splenic	25%	
Renal	26%	66-75%
Cerebrovascular	13%	73-80%

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Segmental Arterial Mediolytic (SAM) vs. Fibromuscular Dysplasia (FMD)

Imaging findings	SAM	FMD
Aneurysm	76%	22-28%
Dissection	60%	17-22%
Rupture	45%	Not reported
String of Beads	15%	60-70%
Occlusion	17%	Not reported

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Segmental Arterial Mediolytic (SAM) vs. Fibromuscular Dysplasia (FMD)

Imaging:			
A: Right internal carotid artery (ICA) dissection (upper arrow) and irregularity (lower arrow)	A		B
B: Right ICA beading appearance			
Histologic findings		Vacuolar degeneration of the arterial media	Fibrous or fibromuscular thickening of the arterial wall

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Summary



Demographics: 143 study pts, median age: 55 years and 67.8% were males



Comorbidities: HTN (42.7%), tobacco abuse (11.9%), HL (11.9%), and DM (1.4%)



Symptoms: abdominal pain (79.7%), intra-abdominal bleeding (49.7%), nausea/vomiting (16.1%), cerebrovascular symptoms (11.9%), melena/ hematochezia (5.6%), diarrhea (4.9%), shock (4.2%), and asymptomatic (4.9%)



Involvement: SMA (53.1%), hepatic (44.8%), celiac (35.7%), renal (25.9%), splenic (24.5%), cerebrovascular involvement (13.3%) and IMA (10.5%)



Pathology: aneurysm (76.2%), dissection (60.8%), rupture (45.5%), stenosis (18.9%), occlusion (16.9%), 'string of beads' (14.7%), thrombosis (14.7%), pseudo-aneurysm (11.9%), and wall thickening (7.7%)

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Summary II



Diagnostic Tools: CT/CTA (59.4%), histology (44.1%) CBA (29.4%), and autopsy (5.6%).

Genetic Testing +/- Pathology: DD: FMD, SAM or vEDS when multiple arteries are involved + beading



Interventions: Coil embolization (27.9%), abdominal organ surgery (23.5%), open arterial repair (20.6%) and angioplasty/stenting (8.1%).



Medical Management: antihypertensive (19.9%), anticoagulation (11.8%), antiplatelet agents (10.3%) and conservative treatment only (8.1%).



Outcome: Improvement (90.6%) of patients with a reported final outcome.
Of the 80 pts who had f/u imaging, 66.3% showed improvement, 17.5% remained unchanged, and 16.3% worsened.

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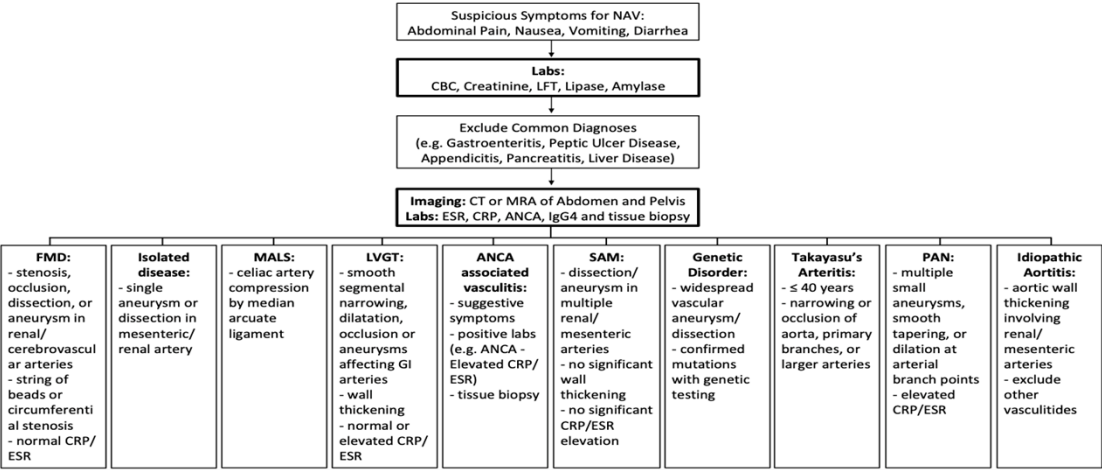


Our Approach

- **Multidisciplinary approach:** Vascular medicine, vascular surgery, IR, general surgery..
- **Careful History and Physical.**
- **Initial Labs:** CBC, CMP, LFT's, lipase, amylase.
- **Images:** CT/CTA or MR/MRA.
- **Exclude Common Diagnoses:** gastroenteritis, pancreatitis, PUD, liver disease.
- **Further Work Up:** ESR/CRP, ANCA, tissue biopsy and genetic testing.
- **Use diagnostic definitions and tools:** Confirmed or presumed diagnoses!
- **Follow up:** based on diagnosis: CTA thin cuts in 1, 3, 6, and 12 months.



Abdominal Vasculopathy Work-up Algorithm



Final Summary

- Non-atherosclerotic abdominal vasculopathies are rare but can be life threatening.
- No consensus on some diagnostic criteria or work up strategy.
- CT angiogram has become the imaging of choice.
- ESR/CRP can be elevated in most pathologies and their role is questionable.
- Role of genetic testing and pathology (multiple pathologies in multiple vessels).



Final Summary II

- Most patients received conservative therapy.
- Endovascular therapy has been more frequently used.
- Most patients have had symptomatic improvement. Improvement on images varied.
- Multidisciplinary approach.
- More research is needed to address gaps in diagnoses and management.



Sunset, Gaza City







Thank You!

Sydney Olson
Jonathan Hyde
Dawn Witt
Ross Garberich

Questions?

