# Anticoagulation Management in Loeys-Dietz Syndrome with Atrial Fibrillation

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## Introduction

- Loeys-Dietz syndrome (LDS): Rare autosomal dominant connective tissue disorder
- Heterozygous mutations along the transforming growth factor-beta (TGFB) signaling pathway
- Associated with multiple vasculopathies, skeletal abnormalities, and other systemic manifestations
- Increased risk for thromboembolic events in connective tissue disorders without evidence-based guidelines for anticoagulation

## Clinical Presentation

66-year-old-male with a PMHx significant for LDS, Thoracic Aortic Aneurysm repair, Aortic Valve repair, HTN, BPH, and Atrial Fibrillation s/p PPM presented with epigastric pain, nausea, vomiting, and bloody diarrhea

## Patient Information

### Medications

Warfarin 7.5 mg

Losartan 100 mg

Metoprolol Succ. XL 200 mg

Doxazosin 4 mg

### Review of Systems

*Non-radiating cramping/burning pain in epigastric area*

*Nausea*

*NBNB vomiting*

*Dark/bloody diarrhea*

### Vitals

**Temperature:** 36.9°C

**Blood Pressure:** 162/97 mmHg

**HR:** 67 beats/min

**RR:** 16 breaths/min

**Pulse Ox:** 97% on RA

### Physical Exam

**GEN:** Alert, awake, oriented
**HEENT:** Atraumatic, normocephalic
**CV:** Normal capillary refill, *diastolic murmur at right upper sternal border*
**RESP:** Aerating well, CTA
**ABD:** *Distended, tender,* soft, normal bowel sounds, no guarding
**EXTREM:** Moves all, no edema
**NEURO:** A&Ox3, no FND

| Labs on Admission | |
|---|---|
| **Hgb** | 13.5 |
| **WBC** | 9.6 |
| **Troponin** | 0.180 |
| **BMP** | WNL |
| **EKG** | Atrial paced rhythm w/ T-wave inversions in anterior leads |
| **CT Abd/Pelvis** | WNL |

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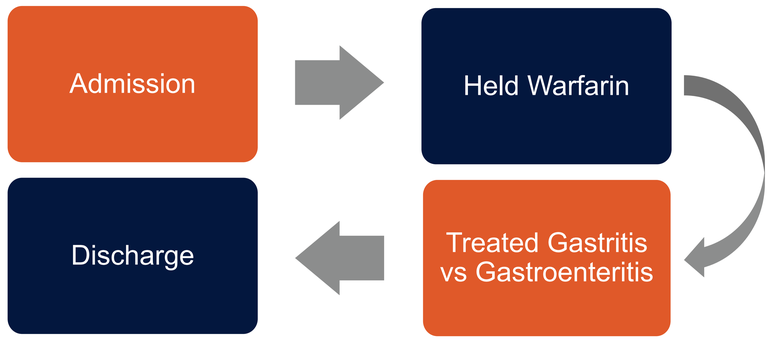
## Hospital Course




## Infographics

| Letter | Risk Factor | Score |
|---|---|---|
| C | Congestive Heart Failure/LV dysfunction | 1 |
| H | Hypertension | 1 |
| $A_2$ | Age ≥ 75 | 2 |
| D | Diabetes mellitus | 1 |
| $S_2$ | Stroke/TIA/thrombo-embolism | 2 |
| V | Vascular disease* | 1 |
| A | Age 65-74 | 1 |
| Sc | Sex category (i.e., female sex) | 1 |

$CHA_2DS_2$-VASc Score; LV dysfunction means LV EF ≤ 40%. Hypertension includes the patients with current antihypertensive medication. *Prior myocardial infarction, peripheral artery disease, aortic plaque. LV: Left Ventricular, TIA: Transient Ischemic Attack

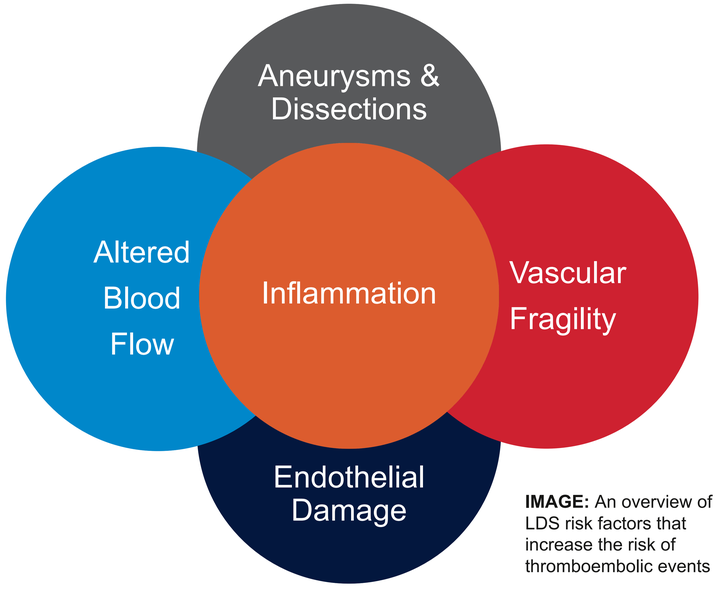



**IMAGE:** An overview of LDS risk factors that increase the risk of thromboembolic events

## Discussion

- Anticoagulation was held in the setting of a suspected GI bleed
- After a GI bleed was ruled out and the patient was subsequently treated, a clinical conundrum was present at the time of discharge
- While our patient's chronic atrial fibrillation is managed with oral anticoagulation, dosing and regimen seem to be unaffected by the underlying rare connective tissue disorder of LDS
- This syndrome often presents with damaged blood vessels, vascular fragility, altered blood flow, arterial aneurysms and dissections, and inflammation which - in totality - activates the clotting cascade, increasing the risk of thrombosis
- Review of literature reveals that this is not limited to the likes of LDS but also habitually characterizes other connective tissue disorders
- As such, this clinical picture raises concerns regarding anticoagulation management of connective tissue disorders, especially in the setting of a thoroughly-studied chronic condition, like that of atrial fibrillation
- Currently, there is a lack of consensus on the use of anticoagulation for prophylaxis of thromboembolic events in connective tissue disorders, let alone in those with concomitant atrial fibrillation
- Thus, management guidelines should be developed in those with varying forms of CTD, especially in the accompaniment of cardiovascular risk factors, provided that the potential benefits outweigh bleeding risks

## Clinical Pearls

- LDS, among other connective tissue disorders, increases the risk for thromboembolic events
- The $CHA_2DS_2$-VASc Score identifies a need for anticoagulation but does not qualify connective tissue disorders as a risk factor
- The lack of guidelines for connective tissue disorders, let alone those with concomitant atrial fibrillation, leaves uncertainty about optimal anticoagulation management

## References

1. Isselbacher E, Preventza O, et al. 2022 ACC/AHA Guideline for the Diagnosis and Management of Aortic Disease. J Am Coll Cardiol. 2022;80(24):e223-e393. doi:10.1016/j.jacc.2022.08.004
2. MacCarrick G, Black JH 3rd, Bowdin S, et al. Loeys-Dietz syndrome: a primer for diagnosis and management. Genet Med. 2014;16(8):576-587. doi:10.1038/gim.2014.11
3. Loeys BL, Chen J, Neptune ER, et al. A syndrome of altered cardiovascular, craniofacial, neurocognitive and skeletal development caused by mutations in TGFBR1 or TGFBR2. Nat Genet. 2005;37(3):275-281. doi:10.1038/ng1511
4. Loeys BL, Schwarze U, Holm T, et al. Aneurysm syndromes caused by mutations in the TGF-beta receptor. N Engl J Med. 2006;355(8):788-798. doi:10.1056/NEJMoa055695
5. Velchev JD, Van Laer L, Luyckx I, Dietz H, Loeys B. Loeys-Dietz Syndrome. Adv Exp Med Biol. 2021;1348:251-264. doi:10.1007/978-3-030-80614-9_11
6. Shi X, Young CD, Zhou H, Wang X. Transforming Growth Factor-β Signaling in Fibrotic Diseases and Cancer-Associated Fibroblasts. Biomolecules. 2020;10(12):1666. Published 2020 Dec 12. doi:10.3390/biom10121666
7. Jung BC, Kim NH, Nam GB, et al. The Korean Heart Rhythm Society's 2014 Statement on Antithrombotic Therapy for Patients with Nonvalvular Atrial Fibrillation: Korean Heart Rhythm Society. Korean Circ J. 2015;45(1):9-19. doi:10.4070/kcj.2015.45.1.9

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