Descriptive Analysis of Real-World Dual-Pathway Inhibition Strategies in Peripheral Artery Disease Post-Vascular Intervention

Yale NewHaven Health

Maia Determan, PharmD; David J. Silva, PharmD, BCCP, BCPS; Heather Lyons, PharmD, BCCP, BCPS; Lionel Picot-Vierra, PharmD, BCCP, BCPS, CACP

Background

- For patients with symptomatic lower extremity peripheral artery disease (LE-PAD), antithrombotic medications are essential for preventing secondary thrombotic vascular events.
- Dual-pathway inhibition with rivaroxaban 2.5 mg twice daily and low-dose aspirin (ASA) after revascularization for symptomatic LE-PAD is supported by the VOYAGER- PAD trial showing a reduction in major adverse cardiovascular and limb events in this population.[1]
- There is a paucity of data describing the use of alternative rivaroxaban dosing regimens or off-label use of other direct oral anticoagulants (DOACs) as a component of dual-pathway inhibition in symptomatic LE-PAD post-vascular intervention.

Canadian Cardiovascular Society 2022 Guidelines for PAD[2]

Recommendation	Strength	Quality
Rivaroxaban 2.5 mg twice daily + low-dose ASA +/- short-term clopidogrel, is recommended for LE-PAD after revascularization	Strong	Endovascular (Moderate) Surgical (High)
For LE-PAD after **urgent** revascularization, we suggest any of: (1) Full-dose anticoagulation + Single antiplatelet therapy (SAPT) (2) Rivaroxaban 2.5 mg twice daily + ASA +/- short-term clopidogrel (3)Dual antiplatelet therapy (DAPT)	Weak	Very-Low

European Society for Vascular Surgery 2020 Clinical Practice Guidelines on the Management of Acute Limb Ischaemia[3]

Recommendation	Strength	Quality
Long term anticoagulation may be considered after thrombectomy or endovascular treatment of a prosthetic bypass graft **occlusion**	Weak	Moderate

Purpose

- The purpose of this study is to describe dual-pathway inhibition prescribing practices at a five-hospital health system in patients with symptomatic LE-PAD, who underwent vascular intervention.

Disclosures: The authors of this presentation have no disclosures concerning possible financial or personal relationships with commercial entities that may have a direct or indirect interest in the subject matter of this presentation.

This project was deemed a clinical quality improvement initiative and IRB review was not required.

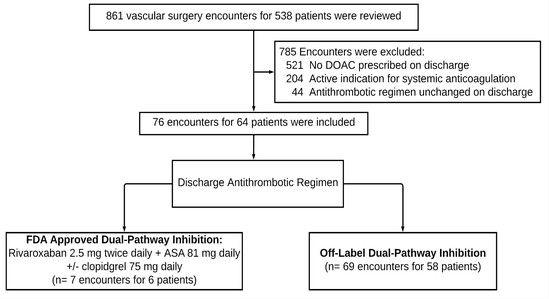
Methods

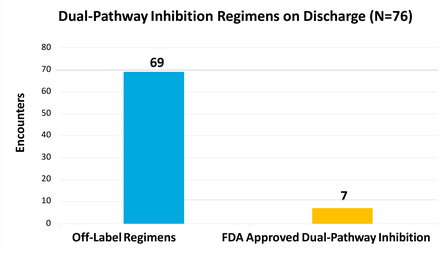
- Electronic medical records of adult patients who underwent revascularization for symptomatic LE-PAD at a five-hospital health system between January 2017 - December 2022 were retrospectively reviewed.
- Inpatient and outpatient vascular surgery hospital encounters for patients discharged on a DOAC as a component of dual-pathway inhibition were included.
- Patients were excluded if having active conditions requiring systemic anticoagulation, and hospital encounters were excluded if no changes were made to maintenance antithrombotic regimens during index hospital encounter.
- Antithrombotic regimens prescribed on hospital discharge after undergoing revascularization for symptomatic LE-PAD are reported for all included hospital encounters. For patients with multiple qualifying encounters, baseline characteristics are reported from the initial included encounter.

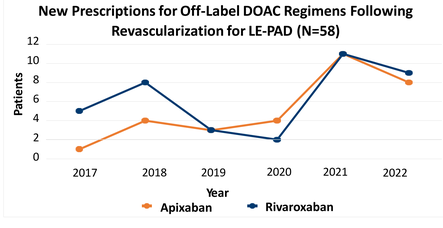
Results

Baseline Characteristics of Patients with Symptomatic LE-PAD Post-Revascularization Prescribed Off-label Dual-Pathway Inhibition

Characteristics	Patients (N=58)
Median age (IQR) - yr	63.9 (58-72.4)
Female sex - no. (%)	21 (32.2)
Median BMI (IQR)	26 (24-30)
Race - no. (%)	
White	39 (67.2)
Black	10 (17.2)
Asian	2 (3.4)
Other	7 (12.1)
Risk factors and coexisting conditions - no. (%)	
Hypertension	43 (74.1)
Hyperlipidemia	34 (58.6)
Current smoker	26 (44.8)
Diabetes mellitus	32 (55.2)
Estimated GFR <60 ml/min/1.73 m^2	18 (31)
Coronary artery disease	27 (46.6)
Known carotid disease	11 (19)
Peripheral artery disease - related history - no. (%)	
Previous amputation	11 (19)
Previous peripheral revascularization	39 (67.2)
Qualifying revascularization - no. (%)	
Performed for claudication	26 (44.8)
Performed for critical limb ischemia	32 (55.2)
Performed for peripheral stent occlusion	15 (25.9)
Performed for bypass graft occlusion	12 (20.7)
Medications on admission - no. (%)	
Statin	48 (82.8)
Aspirin	45 (77.6)
Clopidogrel	33 (56.9)
Oral anticoagulation	11 (19)
Apixaban	6 (10.3)
Rivaroxaban	3 (5.2)
Warfarin	2 (3.4)







DOACs Prescribed as a Component of Off-Label Dual-Pathway Inhibition (N=69)

Apixaban (44.9%)	
5 mg twice daily	14
10 mg twice daily*	9
2.5 mg twice daily	8

**10 mg twice daily x 7 days, then reduced to 5 mg twice daily*

Rivaroxaban (55.1%)	
20 mg daily	13
15 mg twice daily**	12
2.5 mg twice daily	9
10 mg daily	2
15 mg daily	1

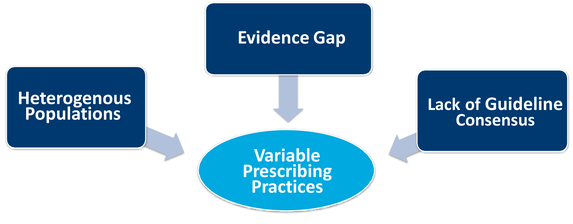
***15 mg twice daily short-term (2 to 30 days), then reduced to 20 mg daily*

Antiplatelets Prescribed as a Component of Off-Label Dual-Pathway Inhibition (N=69)	
DOAC monotherapy	**9**
DOAC + SAPT	**52**
Clopidogrel 75 mg daily	24
ASA 81 mg daily	23
ASA 325 mg daily	3
Prasugrel 10 mg daily	2
DOAC + DAPT	**8**
ASA 81 mg daily + clopidogrel 75 mg daily	5
ASA 325 mg daily + clopidogrel 75 mg daily	3

Conclusions

- A wide range of dual-pathway inhibition strategies were utilized for symptomatic LE-PAD after revascularization, including DOAC monotherapy, DOAC with single antiplatelet, and DOAC with dual antiplatelets, with a minority representing on-label regimens.
- The use of off-label dual-pathway inhibition at our health system has continued to increase over the past six years.
- Understanding our institution-specific prescribing patterns will reveal opportunities for quality improvement, cost-savings, and integration of clinical decision support to aid in safe prescribing practices.

Clinical Implications



- Due to a paucity of high-quality literature in this patient population and inconsistencies across guideline recommendations, the optimal antithrombotic strategy after vascular intervention is not well-established.
- To our knowledge, this is the first report of real-world dual-pathway inhibition dosing strategies in patients with symptomatic LE-PAD after vascular intervention.
- The results of this study may be used to generate questions for further research, including comparative analysis of safety and efficacy of antithrombotic regimens in this population.

References

1. Hiatt WR, Bonaca MP, Patel MR, et al. Rivaroxaban and Aspirin in Peripheral Artery Disease Lower Extremity Revascularization: *Circulation*. 2020;142(23):2219-2230.
2. Primary Panel:, Abramson BL, Al-Omran M, et al. Canadian Cardiovascular Society 2022 Guidelines for Peripheral Arterial Disease. *Can J Cardiol*. 2022;38(5):560-587.
3. Björck M, Earnshaw JJ, Acosta S, et al. Editor's Choice - European Society for Vascular Surgery (ESVS) 2020 Clinical Practice Guidelines on the Management of Acute Limb Ischaemia. *Eur J Vasc Endovasc Surg*. 2020;59(2):173-218.