Real-World Prescription of Dual Pathway Inhibition Therapy in Patients with Peripheral Artery Disease Undergoing Lower Extremity Revascularization

ME Canonico, MD, PhD[1,2], CN Hess, MD, MHS[1,2], S Naveh, MD[1,2], RK Rogers, MD, MSc[1,2], MR Nehler, MD[1,2], SE Hogan, MD MSCS[1,2.3], JA Hsia, MD[1,2], SD Berkowitz, MD[1,2], MP Bonaca, MD, MPH[1,2]

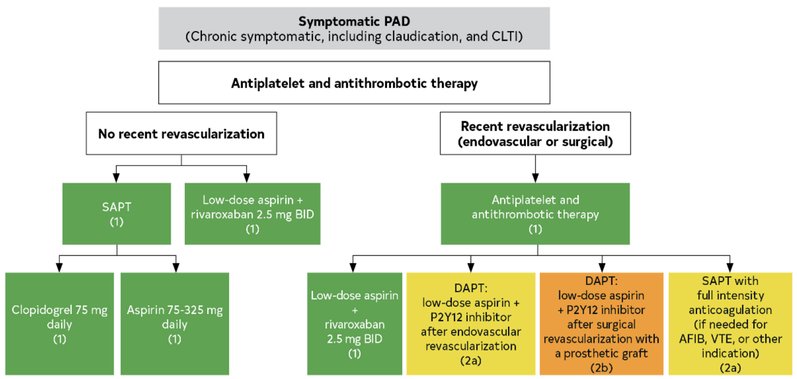
[1] CPC Clinical Research, Aurora, CO, USA, [2] University of Colorado School of Medicine, Aurora, CO, USA, [3] Denver Health and Hospital Authority, Denver, CO, USA

BACKGROUND

VOYAGER PAD trial demonstrated the favorable benefit/risk profile of dual pathway inhibition (DPI) after lower extremity revascularization (LER) due to symptomatic peripheral artery disease (PAD).[1]

The DPI strategy, including aspirin and low-dose rivaroxaban, was approved by the Food and Drug Administration (FDA) in 2021 and has been included such as class 1 indication for patient underwent LER by multisociety lower extremity PAD guidelines in 2024 (figure1).[2] Despite benefits, the real-world prescription of DPI, may be suboptimal and therefore may affect clinical outcomes.

Figure 1. Antithrombotic therapy strategies in patients with symptomatic PAD according to recent revascularization status.



PAD: peripheral artery disease; CLTI: chronic limb-threatening ischemia, BID: bis in die; SAPT: single antiplatelet therapy: DAPT: dual antiplatelet therapy; AP: antiplatelet.

METHODS

Patient encounters with a diagnosis of PAD undergoing LER were selected from TriNetX from Jan 2022 to Dec 2023 in the University of Colorado health system according to ICD-10 and procedure codes as previously described.[3]

PAD encounters were selected according to clinical criteria from VOYAGER-PAD study as listed in table 1.

Table 1. Inclusion and exclusion criteria of PAD encounters undergoing LER.

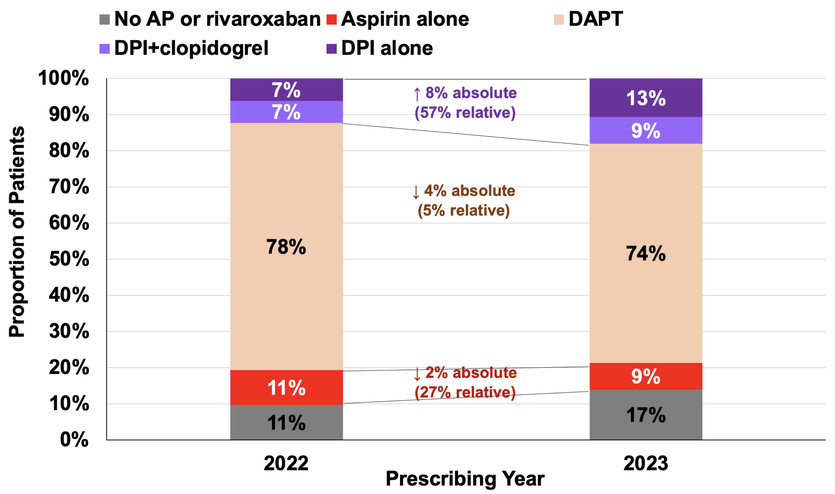
Inclusion	Exclusion
Age ≥ 50 years	Atrial fibrillation or venous thromboembolism
Successful lower extremity revascularization	Advanced CKD with eGFR < 15 ml/min
	Acute coronary syndrome within 30 days
	Intracranial hemorrhage/transient ischemic attack/stroke
	Known history of active malignancy

CKD: chronic kidney disease; eGFR: estimated glomerular filtration rate.

RESULTS

There were 780 encounters for PAD undergoing LER in 2022 and 2023 of which 420 (54%) qualified for VOYAGER PAD. Overall, dual antiplatelet therapy (DAPT) with aspirin and clopidogrel was the most frequent treatment (figure 2), followed by DPI (with or without clopidogrel), aspirin monotherapy, and no recorded antithrombotic. Use of DPI increased 8% in absolute terms (57% relative) from 2022 to 2023 with the majority in 2023 without clopidogrel. Use of DAPT and aspirin monotherapy both decreased from 78% to 74% and 11% to 9%, respectively.

Figure 2. Antithrombotic therapies prescribed to patients affected by peripheral artery disease undergoing lower extremity revascularization in 2022-2023.



DPI: dual pathway inhibition; DAPT: dual antiplatelet therapy; AP: antiplatelet.

DISCLOSURES

DISCUSSION

Patients with PAD undergoing LER are at increased risk for major adverse cardiovascular and limb events.

Despite the FDA approval in 2021 and American Heart Association call to action in 2021, the prescription of antithrombotic therapy after LER remains suboptimal even in 2022-23 in a large, diverse health system. 22% of patients received DPI following LER in 2023. Whether this is because physician inertia, type of provider and service as well as insurance cannot be determined from this dataset.

Targeted efforts are needed to understand barriers for low utilization of antithrombotic therapies in patients underwent LER.

Finally, implementation science studies can help to identify practical and effective approaches to improving outcomes of patients with PAD.

LIMITATIONS

The analysis was conducted on retrospective, albeit recent, pooled observational data which lacked patient level information. In addition, these findings reflect a single, large health system.

CONCLUSION

In 2022-2023, DPI therapy remains underutilized while DAPT results the most frequent antithrombotic regimen after LER; however, the use of DPI is increasing. These data highlight opportunities for implementation science and optimization of antithrombotic therapies after LER.

REFERENCES

1. Bonaca MP, et al. N Engl J Med. 2020 May 21;382(21):1994-2004.
2. Gornik HL, et al. Circulation. 2024 Jun 11;149(24):e1313-e1410.
3. Canonico ME, et al. Vasc Med. 2023 Jun;28(3):233-235.

CONTACT INFO:
Mario Enrico Canonico
email marioenrico.canonico@cpcmed.org

The Authors receive salary support from CPC, a non-profit academic research organization affiliated with the University of Colorado, that receives or has received research grant/consulting funding between July 2021 and July 2023 from the following organizations: Abbot Laboratories, Agios Pharmaceuticals, Inc., Alexion Pharma Godo Kaisha, Amgen Inc., Anthos Therapeutics, Inc., ARCA biopharma, Inc., AstraZeneca Pharma India, AstraZeneca Pharmaceuticals LP, AstraZeneca UK Ltd, AstraZeneca, Produtos Farmaceuticos, Lda, Atentiv, LLC, Bayer, Bayer (Proprietary) Limited, Bayer Aktiengesellschaft, Bayer Pharma AG, Beth Israel Deaconess Medical Center, Better Therapeutics, Boston Clinical Research Institute, LLC, Bristol-Myers Squibb, CellResearch Corporation Pte Ltd, Cleerly, Inc., Colorado Dept of Public Health and Environment, Cook Regentec LLC, CSL Behring LLC, Eidos Therapeutics, Inc., EPG Communication Holdings Ltd., Esperion Therapeutics, Inc, Faraday Pharmaceuticals, Inc., HeartFlow Inc, Insmed, Ionis Pharmaceuticals, IQVIA Inc., Janssen Pharmaceuticals, Inc, Janssen Research & Development, LLC, Janssen Scientific Affairs LLC, Lexicon Pharmaceuticals, Inc., LSG Corporation, MedImmune Limited, Medpace, Inc., Medscape, Merck Sharp & Dohme Corp., Nectero Medical Inc., Novartis Pharmaceuticals Corporation, Novo Nordisk, Osiris Therapeutics, Inc., Pfizer, PPD Development, L.P., Prothena Biosciences Limited, Regeneron, Regents of the University of Colorado (aka UCD), Sanifit Therapeutics S.A., Sanofi, Silence Therapeutics PLC, Stanford University, Stealth BioTherapeutics Inc., The Brigham & Women's Hospital, Inc., Thrombosis Research Institute, University of Colorado Denver, University of Pittsburgh, VarmX, WraSer, LLC.