

# Rivaroxaban in Peripheral Arterial Disease (PAD) Management

Sir,

Patients with peripheral arterial disease (PAD) present from asymptomatic disease to limb-threatening limb ischemia with loss of tissue and gangrene. This disease is quite prevalent, especially in elderly population. However, the true incidence of the disease in Pakistan is unknown. The most common risk factors are diabetes mellitus, hypertension, smoking and male gender. Untreated PAD can result in lifestyle-limiting claudication, limb loss and stroke. Current management of PAD focuses on lifestyle improvement, optimal medical therapy, and supervised exercise therapy.

Atherosclerotic plaque gets complicated with in situ thrombosis or distal thromboembolism. This is due to disruption of plaque surface, adherence and activation of platelets and initiation of the coagulation pathway. Patients are mostly treated with medications to stabilize the at-risk plaque. These include lipid-lowering medications and anti-platelet agents to inhibit coagulation pathways. Despite regular use of these medications, patients develop adverse limb or cardiovascular events. It was suggested that antithrombotic medications can decrease these complications but the evidence for it was lacking. Initial studies using warfarin resulted in increased bleeding complications in patients.

Rivaroxaban is factor Xa inhibitor. It does not need monitoring and has been approved by FDA for the treatment of deep venous thrombosis and arterial thrombosis. It was hypothesized that a low dose of rivaroxaban may decrease thrombotic complications in patients with PAD. COMPASS trial, a randomized controlled trial (RCT), proved this hypothesis.<sup>1</sup>

To see the efficiency of the low dose of rivaroxaban in patients undergoing either surgical or endovascular intervention, VOYAGER trial was conducted.<sup>2</sup> This was a double-blind, multicenter, RCT which enrolled patients undergoing intervention for PAD. Patients treated with rivaroxaban 2.5 mg daily along with aspirin compared with those receiving aspirin only gained a 15% risk reduction in the composite primary efficacy endpoint. This trial provided insight about the potential role of rivaroxaban in managing patients undergoing intervention for PAD. A recently published follow-up study showed that patients in VOYAGER PAD trial who had first adverse limb and cardiovascular events were more at risk of subsequent adverse limb and cardiovascular events despite on standard

medical therapy.<sup>3</sup> It was noted that the addition of low-dose rivaroxaban reduced subsequent adverse limb and cardiovascular events.

By reviewing the current literature, there is mounting evidence to suggest the use of rivaroxaban in managing patients with PAD, especially those who had undergone intervention and have no contraindication for this, although more RCTs are needed to strengthen this evidence. It is also important to conduct RCTs to check the efficacy of rivaroxaban in the Pakistani population before generalizing these results. The cost of direct oral anticoagulants (DOACs) and their compliance must also be considered while advising them.

## COMPETING INTEREST:

The author declared no competing interest.

## AUTHOR'S CONTRIBUTION:

ZR: Conception design of the work, acquisition interpretation of the data, drafting of the initial manuscript, revising, critical analysis, and final approval of the work.

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