Dear Sir,

Retinal vein occlusion (RVO), the second commonest sight-threatening vascular disorder, is a severe pathology characterized by sectoral intraretinal hemorrhages, retinal ischemia, retinal exudates and macular edema. We read with interest the recent editorial of Fateh-Moghadam et al. (1) on the potential effectiveness of antiplatelet therapy in patients with RVO. Despite its frequency, the pathogenesis and risk factors of RVO are not completely understood, and treatments are unsatisfactory due to the inclusion of therapeutic strategies that have not been tested by large, well-designed, prospective, randomised controlled trials (2–4). The effectiveness of the traditional therapeutic armamentarium, including isovolaemic haemodilution, radial optic neurectomy, optic nerve decompression or arteriovenous crossing shunt surgery is limited and is frequently unsuitable for the presence of severe comorbidities, since most patients who develop RVO are older than 50 and the vast majority has associated hypertension, diabetes mellitus, cardiovascular, renal or pulmonary disorders (3, 4). Argon-laser-photocoagulation can prevent the development and treat neovascularizations successfully, but is unable to improve visual function in most cases (5). Finally, vitrectomy combined with either intravenous thrombolysis or arteriovenous shunt surgery may offer promise for central and branch RVO, though this approach still needs further evaluation in larger trials (6).

Basically, the main caveat in the identification of a reliable and effective therapy for this challenging thrombotic disease is our limited understanding of major contributing factors and pathogenesis. It has previously been suggested that platelets may provide a trigger mechanism for venous thrombosis in the eye when local conditions permit (7). In this respect, the article by Leoncini et al. (8) offers a further substantial contribution to this challenging subject by reporting that activated platelets may play a large role in the pathogenesis of RVO. Besides platelet hyperreactivity, a variety of additional risk factors have been variably associated with RVO, including systemic disorders (hypertension, diabetes mellitus, atherosclerosis and hypercholesterolemia), local alterations (increased ocular pressure and open-angle glaucoma) (1, 9), thrombophilic risk factors (factor V Leiden, hyperhomocysteinemia, anticoagulins A and B and type 1 plasminogen activator inhibitor) (10–18), and lipoprotein(a) [Lp(a)]. Lp(a) is an intriguing molecule consisting of a low-density lipoprotein core associated by a disulfide bond to the heterogeneous glycoprotein apolipoprotein(a) [(apo(a)] (19). Due to the high degree of structural homology with plasminogen, apo(a) binds to the lysine-binding sites on fibrin and to membrane proteins of endothelial cells and monocytes, displacing plasminogen and inhibiting fibrinolysis (19, 20). Convincing epidemiological evidence supports a causal role of Lp(a) in several thrombotic disorders, including RVO (21–25) and retinal arteriovenous emboli (26). Since increased fibrin deposition impaired fibrinolysis (21) and platelet activation (8) are hallmarks of RVO, they can both be considered to be potential targets for specific treatments. However, the main question is whether antiplatelet or anticoagulant therapy would provide the highest benefits in both treatment and secondary prevention of RVO. The study by Leoncini et al. (8) prompted clinicians to conduct prospective interventional trials in order to evaluate the role of antiplatelet treatment regimens in RVO patients. We essentially agree with this proposal. Hypothetically, antiplatelet therapy using aspirin would be effective not only because it decreases platelet hyperreactivity, but also because it lowers the plasma concentration of Lp(a) and modulates the influence of Lp(a) on platelets. It was proven that aspirin reduces apo(a) production from hepatocytes via reduction of the transcriptional activity of apo(a) gene with suppression of apo(a) mRNA expression (27), and Lp(a) levels may be decreased after treatment with 81 mg/day of aspirin by up to 20% (28), especially in patients at an increased risk of thrombotic disorders for the presence of high Lp(a) plasma concentrations (29). Recent findings also indicate the involvement of various components of Lp(a) on different underlying pathways concerning platelet activation and aggregation (30, 31), and an enhanced response of platelets via the protease-activated receptor – thrombin receptor has been documented in the presence of Lp(a) (32).

Safe and effective treatments for RVO are currently unavailable (2), hence it is difficult to draw concrete conclusions on this challenging issue (1, 8). Prospective interventional trials with a greater sample size and reliable clinical endpoints are needed to assess the role of antiplatelet therapy in patients with RVO.

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