## Peripheral arterial disease in patients with type 2 diabetes

*To the Editor:*

We thank Katsiki and colleagues for their response (Katsiki, Athyros, Kargaiannis, & Mikhailidis, 2014) to our paper on "Prevalence, incidence and progression of peripheral arterial disease in Asian Indian type 2 diabetic patients" (Eshcol et al., 2014). We agree that non-alcoholic fatty liver disease (NAFLD) and hyperuricemia have been associated with elevated cardiovascular risk and that this could further increase the risk for other complications including peripheral artery disease (PAD). Unfortunately, our study was a retrospective study and not a planned prospective study, and hence, we have not estimated liver enzymes and uric acid levels at baseline and follow up as suggested by the authors, but we would certainly consider doing this in our future prospective studies.

We also agree with the authors that certain drugs like anti hypertensive drugs and lipid lowering agents can influence PAD incidence and outcomes. However, this being a retrospective study, we cannot comment on the specific effects of these drugs on the incidence or progression of PAD in our study.

Finally, we entirely agree with the authors that a multi targeted intervention would be useful in the prevention, development and progression of PAD and such studies are urgently needed, particularly from developing countries where use of such drugs is far less than optimal (Yusuf et al., 2011).

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## Diabetic foot: Lipids, new and old vascular risk markers

*To the Editor:*

We read with interest the meta-analysis by Pei et al. (2014) on the effects of lipids and lipoproteins on the development of diabetic foot in patients with type 2 diabetes mellitus (T2DM). The authors concluded that reduced high density lipoprotein cholesterol (HDL-C) levels were associated with diabetic foot, thus suggesting the importance of targeting HDL-C, and not only low density lipoprotein cholesterol (LDL-C), in T2DM patients.

Statins and fibrates have been previously reported not only to decrease cardiovascular risk and atherogenic dyslipidemia but also to improve the progression, the symptoms and the healing of foot ulcers and to reduce the risk of amputations in diabetic patients (Antonoglou, Papanas, & Maltezos, 2012; Katsiki, Athyros, Karagiannis, & Mikhailidis, 2014; Katsiki et al., 2013; Rajamani et al., 2009). Ezetimibe may decrease atherogenic lipoproteins and improve arterial stiffness in T2DM patients (Katsiki, Theocharidou, Karagiannis, Athyros, & Mikhailidis, 2013; Tsunoda et al., 2013). Of note, endovascular treatment can be useful in terms of ulcer healing in diabetics with critical limb ischemia (Georgakarakos et al., 2013). In this context, the use of lipid-lowering drugs should be taken into consideration in trials of diabetic complications, as stated by Pei et al. (2014).

While agreeing with the authors, we would like to add that there are, apart from lipids, other markers of vascular risk which may have a bearing on the incidence of diabetic complications, such as serum uric acid (SUA) (Katsiki, Papanas, Fonseca, Maltezos, & Mikhailidis, 2013). Indeed, elevated SUA levels have been associated with diabetic peripheral neuropathy (Papanas et al., 2011) and diabetic foot ulcers (Ye et al., 2014). Low plasma bilirubin levels have also been related to the risk of amputation in T2DM patients (Katsiki, Karagiannis, & Mikhailidis, 2013). Moreover, another group has found severe liver fibrosis to be linked with a history of foot ulcer in diabetic patients (de Lédinghe et al., 2012). Therefore, it would be useful to evaluate SUA and bilirubin levels as well as liver enzyme activities in future trials involving patients with diabetic foot lesions. In such patients, these new markers may, if confirmed, prove useful in the prediction of ulceration and amputation.

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