



COMMENT ON PONGRAC BARLOVIC ET AL.

The Association of Severe Diabetic Retinopathy With Cardiovascular Outcomes in Long-standing Type 1 Diabetes: A Longitudinal Follow-up. *Diabetes Care* 2018;41:2487–2494

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We were interested in the recent article by Pongrac Barlovic et al. (1), who showed that severe diabetic retinopathy (SDR) was related to cardiovascular outcomes and peripheral arterial disease in people with type 1 diabetes, even without diabetic kidney disease (DKD). They suggested that adding data on diabetic neuropathy may be interesting. SDR has been related to the risk of lower-extremity amputation in young-onset diabetes (2), but it is not known whether this relationship is independent of DKD.

In Bordeaux University Hospital, we have followed a cohort of patients with type 1 diabetes since 2009, and we have recently shown that diabetic retinopathy could predict their later fast renal decline (3) and cardiovascular events (4). The article by Pongrac Barlovic et al. prompted us to test whether SDR could be related to their later foot ulcers and peripheral neuropathy.

During the year 2009, 204 patients with type 1 diabetes were categorized as to whether they had SDR ($n = 28$, 13.7%) or not. They were mainly men (56.4%), their mean \pm SD age was 51 ± 15 years, BMI was 24.7 ± 3.9 kg/m², duration of diabetes was 21 ± 13 years, and baseline HbA_{1c} was $7.5 \pm 0.9\%$. Their prevalences of arterial hypertension (44.6%), dyslipidemia (35.8% treated by statins), DKD (21.3%), and smoking (25.6%), known risk factors for peripheral arterial disease and neuropathy, were high.

During the interval from 2009 to 2016, 12 subjects experienced a new foot ulcer and 6 had a nontraumatic lower-extremity amputation. For patients with initial SDR, the rates of new ulcers (21.4% vs. 3.4% with no SDR, $P = 0.002$) and amputations (10.7% vs. 1.7% with no SDR, $P = 0.035$) were higher. The relationship between initial SDR and later foot ulcer was significant (odds ratio 2.24, 95% CI 1.11, 4.50) after adjustment for age, sex, height, smoking, HbA_{1c}, duration of diabetes, blood lipids, arterial hypertension, and DKD.

During the intermediate year 2013, the vibration perception thresholds (VPT) at the halluces (Neurothesiometer; Horwell, U.K.) were determined for 138 patients, and the electrochemical sweat conductances (ESC) at the feet (Sudscan; Impéto Médical, France) were determined for 108 patients to assess their nerve function (5). Both measurements were altered for the patients who experienced a foot ulcer (VPT 23 ± 7 V vs. 11 ± 9 V for those with no foot ulcer, $P = 0.004$; ESC 55 ± 4 μ S vs. 74 ± 12 μ S for those with no foot ulcer, $P = 0.007$) and were altered in patients with SDR at baseline: for the VPT, SDR 17 ± 12 V vs. no SDR 11 ± 9 V, $P = 0.011$; for the ESC, SDR 64 ± 20 μ S vs. no SDR 75 ± 10 μ S, $P = 0.001$. The ESC values during 2013 were related to the initial presence of SDR in 2009 ($B = -3.81$, 95% CI -6.48 , -1.20) after adjustment for other predictors as was done for foot ulcers.

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SDR therefore predisposes to foot ulcers and amputations in type 1 diabetes, and we suggest that this association may be mediated by more diabetic peripheral neuropathy. Because Pongrac Barlovic et al. (1) found that SDR predisposes to peripheral arterial disease, special attention must be focused on the prevention of foot ulcers in these subjects, even those without DKD.

Duality of Interest. No potential conflicts of interest relevant to this article were reported.

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