OBJECTIVE — To examine the prospective association of retinal vascular fractal dimension with diabetic retinopathy risk in young people with type 1 diabetes.

RESEARCH DESIGN AND METHODS — This was a hospital-based prospective study of 590 patients aged 12–20 years with type 1 diabetes free of retinopathy at baseline. All patients had seven-field retinal photographs taken of both eyes. Incident retinopathy was ascertained from retinal photographs taken at follow-up visits. Fractal dimension was measured from baseline photographs using a computer-based program following a standardized protocol.

RESULTS — Over a mean ± SD follow-up period of 2.9 ± 2.0 years, 262 participants developed mild nonproliferative diabetic retinopathy (15.0 per 100 person-years). After adjusting for age, sex, diabetes duration, HbA1C, and other risk factors, we found no association between retinal vascular fractal dimension and incident retinopathy.

CONCLUSIONS — Retinal vascular fractal dimension was not associated with incident early diabetic retinopathy in this sample of children and adolescents with type 1 diabetes.
Fractal dimension and retinopathy

Table 1—Relationship between retinal vascular D\(f\) and incident diabetic retinopathy

| Retinal vascular D\(f\) | Incidence per 100 person-years | Model 1* | Model 2† | Model 3‡ |
|------------------------|-------------------------------|----------|----------|----------|
|                        | n                             | HR (95% CI) | P | HR (95% CI) | P | HR (95% CI) | P |
| Right eye only         |                               |           |         |           |         |           |         |
| Quartile 1 (≤1.4497)   | 132                           | 1.00 (Ref) | 0.84 (0.56–1.26) | 0.39 | 0.80 (0.52–1.21) | 0.29 | 0.82 (0.53–1.26) | 0.36 |
| Quartile 2 (1.4498–1.4628) | 132                          | 0.97 (0.65–1.46) | 0.89 | 0.95 (0.62–1.45) | 0.80 | 0.97 (0.63–1.49) | 0.88 |
| Quartile 3 (1.4629–1.4738) | 132                          | 0.95 (0.63–1.45) | 0.82 | 0.90 (0.58–1.40) | 0.64 | 0.93 (0.60–1.45) | 0.75 |
| Quartile 4 (≥1.4739)   | 133                           | 1.00 (Ref) | 0.84 | 0.84 | 0.75 | 0.82 |
| \(P_{\text{trend}}\)  |                               |           |         |         |         |         |
| Right and left eyes combined§|                               |           |         |         |         |         |
| Quartile 1 (≤1.4471)   | 279                           | 1.00 (Ref) | 0.89 (0.67–1.18) | 0.41 | 0.88 (0.65–1.19) | 0.41 | 0.90 (0.66–1.21) | 0.47 |
| Quartile 2 (1.4472–1.4598) | 278                          | 0.98 (0.74–1.30) | 0.89 | 0.98 (0.73–1.32) | 0.88 | 0.99 (0.73–1.33) | 0.93 |
| Quartile 3 (1.4599–1.4730) | 266                          | 0.91 (0.67–1.22) | 0.52 | 0.92 (0.68–1.26) | 0.92 | 0.95 (0.69–1.30) | 0.74 |
| Quartile 4 (≥1.4731)   | 257                           | 1.00 (Ref) | 0.82 | 0.84 | 0.89 |
| \(P_{\text{trend}}\)  |                               |           |         |         |         |         |

*Model 1 adjusted for age and sex. †Model 2 adjusted for age, sex, diabetes duration, A1C, mean arterial blood pressure, BMI, and total cholesterol. ‡Model 3 adjusted for variables in model 2 as well as central retinal arteriolar equivalent and central retinal venular equivalent. §Analysis performed using the generalized estimation equation model.

In summary, our data demonstrate no longitudinal association between retinal vascular D\(f\) and risk of developing early diabetic retinopathy in young patients with type 1 diabetes. Further studies with larger sample size and longer follow-up are required to determine whether retinal fractal analysis is useful in predicting more severe levels of diabetic retinopathy and whether similar associations are present in older patients with type 2 diabetes.

Acknowledgments—This study is supported by the National Health and Medical Research Council Grant 475605 (to T.Y.W., K.C.D., and A.J.J.), the Juvenile Diabetes Research Foundation Innovative Grant (to T.Y.W., K.C.D., A.J.J., and N.C.), and the Royal Victorian Eye and Ear Hospital Research Grant (to N.C.).

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

References

1. Macgillivray TJ, Patton N, Doubal FN, Graham C, Wardlaw JM. Fractal analysis...
of the retinal vascular network in fundus images. Conf Proc IEEE Eng Med Biol Soc 2007;2007:6456–6459
2. Mainster MA. The fractal properties of retinal vessels: embryological and clinical implications. Eye 1990;4:235–241
3. Masters BR. Fractal analysis of the vascular tree in the human retina. Annu Rev Biomed Eng 2004;6:427–452
4. Avakian A, Kalina RE, Sage EH, Rambhia AH, Elliott KE, Chuang EL, Clark JI, Hwang JN, Parsons-Wingerter P. Fractal analysis of region-based vascular change in the normal and non-proliferative diabetic retina. Curr Eye Res 2002;24:274–280
5. Daxer A. Characterisation of the neovascularisation process in diabetic retinopathy by means of fractal geometry: diagnostic implications. Graefes Arch Clin Exp Ophthalmol 1993;231:681–686
6. Daxer A. The fractal geometry of proliferative diabetic retinopathy: implications for the diagnosis and the process of retinal vasculogenesis. Curr Eye Res 1993;12:1103–1109
7. Daxer A. Mechanisms in retinal vasculogenesis: an analysis of the spatial branching site correlation. Curr Eye Res 1995;14:251–254
8. Liew G, Wang JJ, Cheung N, Zhang YP, Hsu W, Lee ML, Mitchell P, Tikellis G, Taylor B, Wong TY. The retinal vasculature as a fractal: methodology, reliability, and relationship to blood pressure. Ophthalmology 2008;115:1951–1956
9. Cheung N, Donaghue KC, Liew G, Rogers SL, Wang JJ, Lim SW, Jenkins AJ, Hsu W, Li Lee M, Wong TY. Quantitative assessment of early diabetic retinopathy using fractal analysis. Diabetes Care 2009;32:106–110
10. Donaghue KC, Fung AT, Hing S, Fairchild J, King J, Chan A, Howard NJ, Silink M. The effect of prepubertal diabetes duration on diabetes: Microvascular complications in early and late adolescence. Diabetes Care 1997;20:77–80
11. Maguire A, Chan A, Cusumano J, Hing S, Craig M, Silink M, Howard N, Donaghue K. The case for biennial retinopathy screening in children and adolescents. Diabetes Care 2005;28:509–513
12. Mohsin F, Craig ME, Cusumano J, Chan AK, Hing S, Lee JW, Silink M, Howard NJ, Donaghue KC. Discordant trends in microvascular complications in adolescents with type 1 diabetes from 1990 to 2002. Diabetes Care 2005;28:1974–1980
13. Cheung N, Rogers SL, Donaghue KC, Jenkins AJ, Tikellis G, Wong TY. Retinal arteriolar dilation predicts retinopathy in adolescents with type 1 diabetes. Diabetes Care 2008;31:1842–1846
14. Rogers SL, Tikellis G, Cheung N, Tapp R, Shaw J, Zimmet PZ, Mitchell P, Wang JJ, Wong TY. Retinal arteriolar caliber predicts incident retinopathy: the Australian Diabetes, Obesity and Lifestyle (AusDiab) study. Diabetes Care 2008;31:761–763
15. Nguyen TT, Wang JJ, Sharrett AR, Islam FM, Klein R, Klein BE, Cotch MF, Wong TY. Relationship of retinal vascular caliber with diabetes and retinopathy: the Multi-Ethnic Study of Atherosclerosis (MESA). Diabetes Care 2008;31:544–549