Is the pulse rate useful in assessing risk of diabetic retinopathy and macular oedema? The Wisconsin Epidemiological Study of Diabetic Retinopathy

Tien Yin Wong, Scot E Moss, Ronald Klein, Barbara E K Klein

Abstract

**Aim**—To describe the relation between pulse rate and incident diabetic retinopathy.

**Methods**—Population based cohort study of people with diabetes. Resting pulse rate was measured in 30 second intervals. Diabetic retinopathy was evaluated from masked gradings of fundus photographs.

**Results**—People with higher pulse rates were more likely to have 4 year progression of retinopathy, progression to proliferative retinopathy, and incident macular oedema than those with lower pulse rates. However, these associations were attenuated after controlling for blood pressure, glycosylated haemoglobin, and other risk factors.

**Conclusion**—Pulse rate may be a clinical indicator of overall risk of diabetic retinopathy, but is not independently associated with the condition.

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The pulse rate reflects cardiovascular health and disease in people with, and without, diabetes. Increased pulse rate appears to be associated with various cardiovascular conditions (such as risk of atherosclerosis, hypertension, cardiovascular diseases, and mortality) and possibly to metabolic alterations related to obesity, glucose regulation, and insulin resistance. Because a number of these are also related to development and progression of diabetic retinopathy, it has been suggested that the pulse rate may be clinically useful in the assessment of retinopathy risk in people with diabetes.

In Wisconsin Epidemiological Study of Diabetic Retinopathy (WESDR), we had previously found inconsistent cross sectional associations between a higher pulse rate and prevalent diabetic retinopathy. Longitudinal data are now available for further analysis. Thus, the intent of this study is to examine the association between pulse rate and the 4 year incidence and progression of diabetic retinopathy in the WESDR cohort.

**Materials and methods**

The population, procedures, and results of the WESDR are found in detail elsewhere. Briefly, stereoscopic colour fundus photographs of seven standard fields of each eye were taken, and graded in a masked fashion for retinopathy using the ETDRS adaptation of the modified Airlie House classification system. Level 10 represents no retinopathy; levels 21, 31, 37, 43, and 53 represent increasing severity of non-proliferative retinopathy; and levels 60 and higher represent proliferative retinopathy. Combining scores for both eyes, weighted for worse eye, results in a 15 step scale of retinopathy level for a person. Incidence of any retinopathy was estimated from people who had no retinopathy at baseline and who participated in the follow up examination. Progression to proliferative retinopathy was estimated from all people free of this at baseline who participated in the follow up examination. For people with no or only non-proliferative retinopathy, progression was defined as an increase in the severity of retinopathy by two steps or more from the baseline level at follow up. Presence of macular oedema was defined as thickening of the retina with or without partial loss of transparency within one disc diameter from the centre of the macula according to ETDRS criteria. The incidence of macular oedema was estimated from all people who had no macular oedema and had not been previously treated with photocoagulation at baseline who participated in the follow up examination.

**Results**

At baseline, the mean pulse rate was 80.7 (SD 13.9) beats per minute, higher in younger onset (84.0 (14.0)) than older onset diabetes (78.5 (13.3)). The mean baseline pulse rate...
was similar between participants and non-participants in the 4 year examination (data not shown). In logistic regression models, increasing pulse rates were associated with higher 4 year rates of progression in retinopathy, progression to proliferative retinopathy and incidence of macular oedema, but not incidence of retinopathy (Table 1). However, after controlling for age, duration of diabetes, retinopathy at baseline, systolic blood pressure, and glycosylated haemoglobin levels (variables independently related to retinopathy or macular oedema in previous reports5–9), these associations became statistically non-significant after controlling for known retinopathy risk factors. From a clinical perspective, while measurements of pulse rate in diabetic people may be an abnormally high pulse rate has been hypothesised to be a marker of various atherosclerosis risk factors, and may even be a pathophysiological factor in the genesis of atherosclerosis itself.10 Another hypothesis is that pulse rate reflects disturbances in the autonomic nervous system, possibly the excess of sympathetic activity seen in people with hypertension, increased cardiovascular workload, and insulin resistance.4 As diabetic retinopathy and macular oedema may also be related to similar vascular, metabolic, and autonomic nervous system disturbances,6–9 the associations between pulse rate and retinopathy observed in WESDR are not unexpected.

Because pulse rate is correlated with mortality,1–4 survival bias was a concern. Survival bias may occur if people with higher pulse rates were more likely to die before the 4 year follow up (censored observations) and also more likely to develop retinopathy or macular oedema. However, as baseline pulse rates were similar between participants and non-participants of the 4 follow up examinations, survival bias was unlikely to be significant.

In conclusion, in people with diabetes, a higher pulse rate appears to be associated with an elevated pulse rate was associated with 4 year progression of diabetic retinopathy, progression to proliferative retinopathy, and incident macular oedema. However, these associations became statistically non-significant after controlling for known retinopathy risk factors. Thus, it appears that pulse rate is an overall indicator of these and possibly other una- measured factors related independently to risks of retinopathy and macular oedema in people with diabetes.

The underlying biological basis for many of these observations is not clear. Nevertheless, an abnormally high pulse rate has been hypothesised to be a marker of various atherosclerosis risk factors, and may even be a pathophysiological factor in the genesis of atherosclerosis itself. Another hypothesis is that pulse rate reflects disturbances in the autonomic nervous system, possibly the excess of sympathetic activity seen in people with hypertension, increased cardiovascular workload, and insulin resistance. As diabetic retinopathy and macular oedema may also be related to similar vascular, metabolic, and autonomic nervous system disturbances, the associations between pulse rate and retinopathy observed in WESDR are not unexpected.

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provide some information regarding overall risk of retinopathy, it is unlikely to be as important as measuring blood pressure or glycosylated haemoglobin levels.

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