RESEARCH

Association of obesity with diabetic retinopathy in US adults with diabetes in a national survey

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Abstract

Objective: There is a lack of consensus on whether a high BMI increases the risk of diabetic retinopathy (DR). We aimed to investigate the association between BMI, overweight, obesity, and DR using the data of diabetes respondents in the 2015 US Behavioral Risk Factor Surveillance System survey.
Methods: Diabetes respondents aged over 18-year-old with complete information as well as undergone fundus examination in the past 2 years or had been diagnosed with DR were included. Weighted logistic regression analyses were used to identify the association of BMI with DR.
Results: Among the 21,647 diabetes respondents, 4588 respondents had DR with a weighted prevalence of 22.5%. The mean BMI of all diabetes respondents was 31.50 ± 6.95 kg/m^2 with 18,498 (86.5%) overweight and 11,353 (54.6%) obese. The mean BMI of the DR group (31.83 ± 7.41 kg/m^2) was significantly higher than that of the non-DR group (31.41 ± 6.81 kg/m^2, $P < 0.05$). The proportion of obese respondents in the DR group was higher than the non-DR group (54.3%, $P < 0.001$). The weighted prevalence of DR was 0.8, 13.8, 29.7, and 55.7% for the emaciation group, the normal weight group, the overweight group, and the obesity group, respectively ($P < 0.001$). Weighted logistic regression analysis showed that both BMI (adjusted OR = 1.004, 95% CI 1.003–1.004) and obesity (adjusted OR = 1.051, 95% CI 1.048–1.055) were associated with DR after adjusting for the confounding variables. However, overweight was not significantly associated with DR.
Conclusion: The prevalence of DR in the normal weight, overweight, and obesity groups increased gradually. Obesity, rather than overweight, was significantly associated with increased DR prevalence.

Key Words
- diabetes
- diabetic retinopathy
- obesity
- overweight
- risk factor

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Introduction

Diabetic retinopathy (DR), a typical microvascular complication of diabetes mellitus (DM), is the leading cause of blindness in adult patients aged 20–74 years old in developed countries (1). In the US, about 4.2 million DM patients aged over 40-year-old had DR (https://www.aao.org/ppp. Accessed 15 September 2020). Every year, about 23,000 patients had permanent blindness caused by DM, and their average medical expense was about USD 500 million (2).

Multiple risk factors lead to DR. The prevalence of DR increases as DM is prolonged. Strikingly, over 50% of the DM patients with a duration of over 20 years developed DR (3). Long course, poor glucose control, hypertension, and hyperlipidemia have been recognized as the major risk factors of DR (1, 4, 5, 6). In addition, a high BMI might be associated with DR (7, 8), although some studies suggested that a high BMI did not increase the risk of DR. According to the Wisconsin epidemiologic study of DR (WESDR),

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obesity was not associated with the high incidence of DR in DM patients with older-onset diabetes (9). The prevalence of DR was lower in patients with a higher BMI, according to the Singapore Malay Eye Study (SiMES) on 718 DM patients conducted in Singapore (10).

Obesity is a risk factor of diabetic nephropathy (11, 12). DR and diabetic nephropathy had common pathogenesis mechanisms. Currently, there is a lack of consensus on whether a high BMI increases the risk of DR. The ongoing Behavioral Risk Factor Surveillance System (BRFSS) is a health-related telephone survey conducted in the US, in which over 20,000 DM respondents were included. To investigate whether a high BMI is associated with DR in DM patients and whether overweight/obesity is associated with the increased prevalence of DR, We analyzed the data of DM respondents in the US BFRSS survey to identify the correlation between BMI, overweight/obesity, and DR.

Methods

BRFSS is the health-related telephone surveys conducted in the US, which collects data about the residents regarding health-related risk behaviors, use of preventive services and chronic health conditions. More than 400,000 adult interviews complete every year, making it the largest health survey system in the world. All the data were collected from interviews conducted both by landline telephone and cellular telephone (https://www.cdc.gov/brfss/about/index.htm. Accessed 30 August 2020).

The BRFSS data were de-identified. The data were publicly available from the US Centers for Disease Control and Prevention website.

Questions used in this study in the 2015 BRFSS survey include age, race, education, body height, body weight, education, current smoking and chronic disease history. Age (<45 years or ≥45 years), education, race, ethnicity (Hispanic, Latino/a, or Spanish origin or no), and current smoking were categorized according to the original variables in the questionnaire. With the shoes off, net body height and weight were reported by the respondents. The BMI was calculated as follows: BMI (kg/m^2)=weight/height squared. Based on the BMI level, respondents were grouped into the emaciation group (BMI <18.5 kg/m^2), the normal weight group (18.5 kg/m^2 < BMI <25 kg/m^2), the overweight group (BMI ≥25 kg/m^2), and the obesity group (BMI ≥30 kg/m^2).

The chronic disease status of the respondents was self-reported. In case a respondent answered 'Yes' to 'has a doctor, nurse, or other health professional ever told you have diabetes', the respondent was defined as a respondent with DM, excluding gestational diabetes, pre-diabetes, and borderline diabetes. Hypertension was defined if a respondent answered 'Yes' to 'ever been told by a doctor, nurse or other health professional that you have high blood pressure', excluding gestational hypertension and borderline hypertension. Hypercholesterolemia was defined if a respondent answered 'Yes' to 'ever been told by a doctor, nurse or other health professional that your blood cholesterol is high'. When a respondent answered 'Yes' to 'has a doctor ever told you that diabetes has affected your eyes or that you had retinopathy', the respondent was defined as a subject with DR. A respondent with coronary heart disease and/or stroke was defined as a subject with cardiovascular disease (CVD).

The DM respondents with complete body weight and height information, who had undergone fundus examination in which the pupils were dilated in the past 2 years or had been diagnosed with DR but had not undergone fundus examination in the past 2 years, were included in this study. On the other hand, 3597 respondents undergoing fundus examination in which the pupils were dilated in the past 2 years who refused to answer questions or failed to answer the questions clearly were excluded.

Statistical analysis

All the records in the 2015 BRFSS data were weighted using raking weighting methodology (https://www.cdc.gov/brfss/annual_data/2015/pdf/weighting_the-data_webpage_content.pdf. Accessed August 30 2020). Final weights were assigned to every respondent. SPSS 25.0 software was used for the statistical analysis. The prevalence of chronic diseases was weighted. Weighted chi-squared test was used to analyze the association between DR prevalence and other factors, such as gender, overweight, obesity and chronic diseases. Weighted logistic regression was used to analyze the association between BMI, overweight, obesity and DR with DR as the dependent variable, and BMI, overweight and obesity as the independent variables.

Results

Demographic characteristics

A total of 21,647 DM respondents, including 10,118 males and 11,529 females, were enrolled in this study. Among them, 4588 had DR, and the DR weighted prevalence was

22.5%. The mean BMI was 31.50 ± 6.95 kg/m^2 for all DM respondents. There were 18,498 respondents who were overweight, and the weighted prevalence was 86.5%. There were 11,353 obese respondents with a weighted prevalence of 54.6%.

Compared to non-DR respondents, the DR respondent cohort consisted of more males (57.2%) than females, and more respondents were aged below 45-year-old. About 10.7% of the DR respondents were Latino, higher than the respondents without DR (6.7%, $P < 0.001$). A large proportion of DM respondents (30.1%) in the DR group received only primary or middle school education, and 17.4% in the DR group were current smokers (Table 1).

The mean BMI of the DR group was 31.83 ± 7.41 kg/m^2, significantly higher than that of the non-DR group (31.41 ± 6.81 kg/m^2, $P < 0.05$). The DR group consisted of 55.7% obese respondents, which was higher than the non-DR group (54.3%, $P < 0.001$). The prevalence of overweight in the DR group was slightly lower than that in the non-DR group (Table 1). Based on the BMI level, respondents were grouped into the BMI < 18.5kg/m^2 group, the 18.5 kg/m^2 < BMI < 25 kg/m^2 group, the 25 kg/m^2 ≤ BMI < 30 kg/m^2 group, and the BMI ≥ 30 kg/m^2 group. Results showed that the prevalence of DR increased gradually with the increase in BMI, and it was 0.8, 13.8, 29.7, and 55.7% for the four groups described above, respectively ($\chi^2 = 12{,}498.933$, $P < 0.001$).

DR respondents were more prone to hypertension and hypercholesterolemia (80.0, 68.8%, respectively, $P < 0.001$). About 52.7% of the DR respondents received insulin therapy, which was more than the non-DR respondents (28.0%, $P < 0.001$), and more DR respondents (1737/4588, 36.7%) had CVD than non-DR respondents.

Weighted logistic analysis

According to the weighted logistic regression analysis, with DR as the dependent variable and BMI as the independent variable, BMI was associated with DR (crude OR = 1.005, 95% CI 1.005–1.005, $P < 0.001$) Moreover, after adjusting for possible confounding factors, such as gender, age ≥45 years, hypertension, hypercholesterolemia, insulin therapy,

Table 1 Clinical characteristics between the diabetic retinopathy group and the non-diabetic retinopathy group.

	Non-DR ($n = 17{,}059$)	**DR** ($n = 4588$)	**Total** ($n = 21{,}647$)	χ^2	*P*
Male, *n* (weighted %)	7797 (50.7%)	2321 (57.2%)	10,118 (52.2%)	24,921.536	<0.001
Female, *n* (weighted %)	9262 (49.3%)	2267 (42.8%)	11,529 (47.8%)		
BMI (kg/m^2)	31.41 ± 6.81	31.83 ± 7.41	31.50 ± 6.95	−44.481 (*t* value)	<0.001
BMI ≥25 kg/m^2, *n* (weighted %)	14,583 (86.8%)	3915 (85.4%)	18,498 (86.5%)	2458.965	<0.001
BMI ≥30 kg/m^2, *n* (weighted %)	8901 (54.3%)	2452 (55.7%)	11,353 (54.6%)	1125.938	<0.001
Age ≥45 years, *n* (weighted %)	16,241 (90.6%)	4349 (89.2%)	20,590 (90.3%)	3787.331	<0.001
Hypercholesterolemia, *n* (weighted %)	11,292 (66.1%)	3171 (68.8%)	14,463 (66.7%)	5091.487	<0.001
Hypertension, *n* (weighted %)	13,020 (74.8%)	3694 (80.0%)	16,714 (76.0%)	21,690.367	<0.001
Current smoking, *n* (weighted %)	1909 (12.8%)	676 (17.4%)	2585 (13.8%)	26,781.791	<0.001
Hispanic, Latino/a, or Spanish origin	877 (6.7%)	358 (10.7%)	1235 (7.6%)	33,162.906	<0.001
Education				86,097.351	<0.001
Did not graduate high school	1620 (16.9%)	726 (30.1%)	2346 (18.7%)		
Graduated high school	5392 (32.5%)	1542 (22.6%)	6934 (32.5%)		
Attended college or technical school	4872 (31.0%)	1250 (21.2%)	6122 (30.5%)		
Graduated from college or technical school	5147 (19.7%)	1059 (16.7%)	6206 (18.3%)		
Taking insulin	4815 (28.0%)	2481 (52.7%)	7296 (33.6%)	411,014.913	<0.001
Race				71,438.710	<0.001
White	13,260 (75.0%)	3128 (66.0%)	16,388 (73.0%)		
Black or African American	2414 (18.8%)	853 (24.3%)	3267 (20.0%)		
American Indian or Alaskan Native	322 (1.9%)	154 (2.5%)	476 (2.0%)		
Asian	387 (2.2%)	154 (2.9%)	541 (2.3%)		
Native Hawaiian or other Pacific Islander	141 (0.4%)	92 (0.6%)	233 (0.4%)		
Other race	270 (1.7%)	117 (3.5%)	387 (2.1%)		
No preferred race	39 (0.1%)	10 (0.2%)	49 (0.1%)		
Multiracial	1 (0.0%)	0 (0.0%)	1 (0.0%)		
Stroke, *n* (weighted %)	1432 (7.9%)	725 (16.1%)	2157 (9.8%)	114,661.938	<0.001
Coronary heart disease, *n* (weighted %)	3454 (19.7%)	1439 (31.1%)	4893 (22.3%)	111,317.716	<0.001
Heart attack, *n* (weighted %)	2320 (12.9%)	1046 (22.0%)	3366 (15.0%)	97,937.847	<0.001
Cardiovascular disease, *n* (weighted %)	4262 (24.2%)	1737 (36.7%)	5999 (27.0%)	12,0354.646	<0.001

DR, diabetic retinopathy.

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Latino, education, race, and smoking were adjusted, BMI was still associated with DR (adjusted OR = 1.004, 95% CI 1.003–1.004, $P < 0.001$). Male, hypertension, hypercholesterolemia, and age <45 years were also identified as significant factors associated with DR.

Furthermore, the results of the weighted logistic regression analysis with obesity as the independent variable showed that obesity was related to DR (crude OR = 1.057, 95% CI 1.053–1.060, $P < 0.001$), while after the confounding factors, such as hypertension, hypercholesterolemia, gender, age ≥45 years, insulin therapy, Latino, education, race, smoking were adjusted, obesity remained as a significant factor associated with DR (adjusted OR = 1.051, 95% CI 1.048–1.055, $P < 0.001$). Hypertension, hypercholesterolemia, and age <45 years were also significant factors.

However, the results of the weighted logistic regression analysis with overweight as the independent variable showed that overweight might be a protective factor for DR as compared to BMI<25 kg/m^2 (crude OR = 0.891, 95% CI 0.886–0.895, $p < 0.001$). After possible confounding factors, such as hypertension, hypercholesterolemia, gender, age ≥45 years, insulin therapy, Latino, education, race, and smoking, were adjusted, the adjusted OR was 0.926 (95% CI 0.921–0.930, $p < 0.001$).

Discussion

Among 21,647 DM respondents in the 2015 BRFSS survey, aged over 18-year-old, the weighted prevalence of DR was 22.5%. The BMI of DR respondents was higher than that of non-DR respondents. The prevalence of DR gradually increased with the increase in BMI, while compared to the emaciation group, the prevalence of DR in the normal weight, overweight, and obesity groups increased gradually. Obesity, rather than overweight, was associated with the increased DR prevalence, even after confounding factors were adjusted.

DR is the main cause of blindness in DM patients, and studies on the risk factors are clinically significant. In the current study, BMI was associated with the prevalence of DR. Although the correlation between BMI and DR has been elucidated, a consensus is yet lacking. A previous study in 1993 on 110 Japanese DM patients, aged over 60-year-old, did not show any correlation between BMI and DR (13). In an epidemiological study conducted in Wisconsin (WESDR) on DR, 1370 patients diagnosed with DM after the age of 30 years were grouped as underweight, normal weight, overweight, and obesity groups. The data showed that underweight was related to the incidence of DR compared to the normal weight (9). A cross-sectional study in Croatia included 107 type 2 DM (T2DM) patients did not establish a correlation between BMI and the prevalence of DR (14). Subsequently, 193 T2DM patients aged 50- to 74-year-old were analyzed in the Hoorn study for the risk factors related to DR. The result showed that compared to BMI < 24.5 kg/m^2 DM patients, BMI 25.5–28.4 kg/m^2 DM patients had no higher risk of DR, while BMI > 28.4 kg/m^2 DM patients had a high risk, suggesting that obesity was related to the prevalence of DR, which is consistent with our findings (15). Another study carried out by the Australian Diabetes Management Program (DMP) included 492 DM patients aged 18 years or older from Royal Victorian Eye and Ear hospital and showed a 65.2% prevalence of DR. Moreover, after the confounding factors were adjusted, obesity, but not overweight, was related to the prevalence of DR (8). The Sankara Nethralaya Diabetic Retinopathy Epidemiology and Molecular Genetics Study (SN-DREAMS-I) in Indian, including 1414 DM patients in a cross-sectional analysis, showed that BMI ≥ 23 kg/m^2 was a protective factor for DR (16). A study in Singapore National Eye Centre on 420 Asian DM patients also showed that a high BMI was a protective factor for DR. Compared to BMI < 25 kg/m^2, obesity (BMI ≥ 30 kg/m^2), rather than overweight (BMI 25–29.9 kg/m^2), was the protective factor for DR, while when the cut-off point for overweight/obesity was similar to that for the Asian population, that is, overweight was defined as BMI 23–27.5 kg/m^2 and obesity was defined as BMI > 27.5 kg/m^2; neither obesity nor overweight was found to be associated with DR (17).

People with a high BMI often develop chronic metabolic abnormalities, such as hypertension and hyperlipidemia, which might be the reason for the association of high BMI with DR. The current study showed that the weighted prevalence of hypertension in obese respondents was 81.2% and that of hypercholesterolemia was 68.8%, both higher than that in non-obesity respondents. Obesity was still related to the prevalence of DR after hypertension and hypercholesterolemia were adjusted, suggesting obesity might be related to the increased prevalence of DR in addition to known risk factors, such as hypertension and hypercholesterolemia. In a clinical study on bariatric surgery with Roux-en-Y gastric bypass in DM patients, Roux-en-Y gastric bypass in DM patients delayed the occurrence of DR (18), suggesting that obesity was related to DR. Insulin resistance is commonly related to obesity, which is one of the main mechanisms of DM (19). Obesity-related insulin resistance itself was also found to be associated with DR (20). Obesity-induced inflammation

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and adipose tissue dysfunction might also play a role in the pathogenesis of DR (20). However, the specific mechanism remains unknown.

The definitions of overweight and obesity vary among studies with respect to the correlation between DR and overweight/obesity, which might underlie the varied results. For example, in the WESDR study, overweight was defined as BMI 27.8–31.0 kg/m^2 for males and 27.3–32.2 kg/m^2 for females, and obesity was defined as BMI >31.0 kg/m^2 for males and BMI >32.2 kg/m^2 for females (9). In Australian DMP study, overweight was defined as BMI 25–29.9 kg/m^2 and obesity was defined as BMI >30 kg/m^2 (8). In the Indian SN-DREAMS-I study, obesity was defined as BMI ≥23 kg/m^2 (16), which in some studies on the Asian population, was defined as overweight (21, 22), referring to both the overweight and the obesity populations. Moreover, the mean BMI of patients included in different studies is also varied due to different populations and races. The mean BMI of included patients in Australian DMP studies was greater than 30 kg/m^2 (8), while that in Indian SN-DREAMS-I study was about 25 kg/m^2 (16), in Singapore National Eye Centre study was 25.7 kg/m^2 (17), and that in the Hoorn study on DM patients was 28.7 kg/m^2 (15). This is also a cause for the inconsistency in the results. Therefore, studies on the association between DR and overweight/obesity might present different results if overweight/obesity is defined by the mean BMI of study subjects. Consequently, some studies showed that mild overweight was not related to DR, while severe overweight, that is, obesity, was related to DR (17). The current study subjects had a mean BMI of 31 kg/m^2 and were grouped as follows: emaciation, normal weight, overweight, and obesity. The analysis results showed that the prevalence of DR increased gradually with the increase in BMI and that BMI was related to DR when used as a continuous variable in the weighted logistic regression analysis. Also, obesity was related to the increased prevalence of DR when used as an independent variable.

Nevertheless, the present study had some limitations. First, the type of DM was not defined. The included respondents were type 1 diabetes or T2DM. Second, the study data were based on telephone investigations. The body height and weight of the respondents were self-reported, which might not conform to the actual situation. And there was a lack of laboratory measurement results, such as glycosylated hemoglobin, insulin and lipid profiles. Finally, The DR staging was not known as there was no information of the fundus-associated staging diagnosis in the BRFSS survey. The included subjects were DR respondents who had undergone fundus examination in the past 2 years or had been definitely diagnosed with DR to ensure the accuracy of DR diagnosis. This might result in the underestimation of the prevalence of DR as some patients might have had DR but had not undergone fundus examination due to the lack of obvious clinical symptoms.

In the 2015 BRFSS survey data with 21,647 adult DM respondents, the BMI of DR respondents was higher than that of non-DR patients. The prevalence of DR in the normal weight group, overweight and obesity groups increased gradually compared to the emaciation group. Obesity, rather than overweight, was associated with the increased DR prevalence, suggesting that DM patients with obesity should pay more attention to DR detection and control of risk factors.

Declaration of interest

The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the research reported.

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References

1 American Diabetes Association. 11. Microvascular complications and foot care: standards of Medical Care in Diabetes-2019. *Diabetes Care* 2019 **42** S124–S138. (https://doi.org/10.2337/dc19-S011)

2 Zhang X, Beckles GL, Chou CF, Saaddine JB, Wilson MR, Lee PP, Parvathy N, Ryskulova A & Geiss LS. Socioeconomic disparity in use of eye care services among US adults with age-related eye diseases: National Health Interview Survey, 2002 and 2008. *JAMA Ophthalmology* 2013 **131** 1198–1206. (https://doi.org/10.1001/jamaophthalmol.2013.4694)

3 Tapp RJ, Shaw JE, Harper CA, de Courten MP, Balkau B, McCarty DJ, Taylor HR, Welborn TA, Zimmet PZ & AusDiab Study Group. The prevalence of and factors associated with diabetic retinopathy in the Australian population. *Diabetes Care* 2003 **26** 1731–1737. (https://doi.org/10.2337/diacare.26.6.1731)

4 Klein R. Hyperglycemia and microvascular and macrovascular disease in diabetes. *Diabetes Care* 1995 **18** 258–268. (https://doi.org/10.2337/diacare.18.2.258)

5 Leske MC, Wu SY, Hennis A, Hyman L, Nemesure B, Yang L, Schachat AP & Barbados Eye Study Group. Hyperglycemia, blood pressure, and the 9-year incidence of diabetic retinopathy: the Barbados Eye Studies. *Ophthalmology* 2005 **112** 799–805. (https://doi.org/10.1016/j.ophtha.2004.11.054)

6 Chew EY, Davis MD, Danis RP, Lovato JF, Perdue LH, Greven C, Genuth S, Goff DC, Leiter LA, Ismail-Beigi F, *et al*. The effects of medical management on the progression of diabetic retinopathy in persons with type 2 diabetes: the Action to Control Cardiovascular Risk in Diabetes (Accord) Eye Study. *Ophthalmology* 2014 **121** 2443–2451. (https://doi.org/10.1016/j.ophtha.2014.07.019)

7 Henricsson M, Nystrom L, Blohme G, Ostman J, Kullberg C, Svensson M, Scholin A, Arnqvist HJ, Bjork E, Bolinder J, *et al*. The incidence of retinopathy 10 years after diagnosis in young adult

people with diabetes: results from the nationwide population-based Diabetes Incidence Study in Sweden (DISS). *Diabetes Care* 2003 **26** 349–354. (https://doi.org/10.2337/diacare.26.2.349)
8 Dirani M, Xie J, Fenwick E, Benarous R, Rees G, Wong TY & Lamoureux EL. Are obesity and anthropometry risk factors for diabetic retinopathy? The Diabetes Management Project. *Investigative Ophthalmology and Visual Science* 2011 **52** 4416–4421. (https://doi.org/10.1167/iovs.11-7208)
9 Klein R, Klein BE & Moss SE. Is obesity related to microvascular and macrovascular complications in diabetes? The Wisconsin Epidemiologic Study of Diabetic Retinopathy. *Archives of Internal Medicine* 1997 **157** 650–656. (https://doi.org/10.1001/archinte.1997.00440270094008)
10 Lim LS, Tai ES, Mitchell P, Wang JJ, Tay WT, Lamoureux E & Wong TY. C-reactive protein, body mass index, and diabetic retinopathy. *Investigative Ophthalmology and Visual Science* 2010 **51** 4458–4463. (https://doi.org/10.1167/iovs.09-4939)
11 Meguro S, Kabeya Y, Tanaka K, Kawai T, Tomita M, Katsuki T, Oikawa Y, Atsumi Y, Shimada A, Tanaka M, *et al*. Past obesity as well as present body weight status is a risk factor for diabetic nephropathy. *International Journal of Endocrinology* 2013 **2013** 590569. (https://doi.org/10.1155/2013/590569)
12 Maric C & Hall JE. Obesity, metabolic syndrome and diabetic nephropathy. *Contributions to Nephrology* 2011 **170** 28–35. (https://doi.org/10.1159/000324941)
13 Araki A, Ito H, Hattori A, Inoue J, Sato T, Shiraki M & Orimo H. Risk factors for development of retinopathy in elderly Japanese patients with diabetes mellitus. *Diabetes Care* 1993 **16** 1184–1186. (https://doi.org/10.2337/diacare.16.8.1184)
14 Tomic M, Ljubic S, Kastelan S, Gverovic Antunica A, Jazbec A & Poljicanin T. Inflammation, haemostatic disturbance, and obesity: possible link to pathogenesis of diabetic retinopathy in type 2 diabetes. *Mediators of Inflammation* 2013 **2013** 818671. (https://doi.org/10.1155/2013/818671)
15 van Leiden HA, Dekker JM, Moll AC, Nijpels G, Heine RJ, Bouter LM, Stehouwer CD & Polak BC. Blood pressure, lipids, and obesity are associated with retinopathy: the Hoorn Study. *Diabetes Care* 2002 **25** 1320–1325. (https://doi.org/10.2337/diacare.25.8.1320)
16 Raman R, Rani PK, Gnanamoorthy P, Sudhir RR, Kumaramanikavel G & Sharma T. Association of obesity with diabetic retinopathy: Sankara Nethralaya Diabetic Retinopathy Epidemiology and Molecular Genetics Study (SN-DREAMS Report no. 8). *Acta Diabetologica* 2010 **47** 209–215. (https://doi.org/10.1007/s00592-009-0113-8)
17 Man RE, Sabanayagam C, Chiang PP, Li LJ, Noonan JE, Wang JJ, Wong TY, Cheung GC, Tan GS & Lamoureux EL. Differential association of generalized and abdominal obesity with diabetic retinopathy in Asian patients with type 2 diabetes. *JAMA Ophthalmology* 2016 **134** 251–257. (https://doi.org/10.1001/jamaophthalmol.2015.5103)
18 Madsen LR, Bek T & Richelsen B. Diabetic retinopathy in people with Type 2 diabetes and obesity treated by Roux-en-Y gastric bypass compared with non-operated controls: with focus on the role of diabetes remission in a cross-sectional and a 6-year follow-up study. *Diabetic Medicine* 2019 **36** 457–464. (https://doi.org/10.1111/dme.13876)
19 Wondmkun YT. Obesity, insulin resistance, and type 2 diabetes: associations and therapeutic implications. *Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy* 2020 **13** 3611–3616. (https://doi.org/10.2147/DMSO.S275898)
20 Mbata O, Abo El-Magd NF & El-Remessy AB. Obesity, metabolic syndrome and diabetic retinopathy: beyond hyperglycemia. *World Journal of Diabetes* 2017 **8** 317–329. (https://doi.org/10.4239/wjd.v8.i7.317)
21 Kwon I. Angiotensin-converting enzyme gene insertion/deletion polymorphism is not associated with BMI in Korean adults. *Physical Activity and Nutrition* 2020 **24** 24–28. (https://doi.org/10.20463/pan.2020.0005)
22 Lee MH, Jo SH, Kwon S, Park BW, Bang DW, Hyon MS, Baek SH, Han SH, Her SH, Shin DI, *et al*. Impact of overweight/obesity on clinical outcomes of patient with vasospastic angina: from the Vasospastic Angina in Korea Registry. *Scientific Reports* 2020 **10** 4954. (https://doi.org/10.1038/s41598-020-61947-7)

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