KJMS / OPEN ACCESS Print ISSN: 2790-0207 Online ISSN: 2790-0215

Original article

Association between diabetic macular edema and ischemic heart diseases in type 2 Diabetes Mellitus

Moatasm Mushtak Muhammed[1,*], Professor Dr. Hayder Al-Talqani[2]

[1] MBChB. F.I.B.M.S (ophth.) Department of Ophthalmology, Kirkuk, Iraq

[2] MBChB. F.I.B.M.S (ophth.) Department of Ophthalmology College of Medicine / Al-Kufa University, Iraq

Corresponding author Email address: drssmoamen@gmail.com

DOI: 10.32894/kjms.2021.169713

Abstract:

- ***Background***: Diabetic macular edema (DME) is a major cause of visual impairment in patients with diabetes mellitus. Systemic vascular diseases, such as ischemic heart disease (IHD), may influence the severity of DME. This study aimed to evaluate the association between IHD and DME in patients with type 2 diabetes mellitus by assessing visual acuity, central macular thickness (CMT), and macular cystoid changes using optical coherence tomography (OCT).
- ***Methods:*** This study included 128 patients with type 2 diabetes mellitus, divided into two groups: Group 1 (64 patients) with IHD and Group 2 (64 patients) without IHD. Visual acuity, cystoid macular edema, and CMT were evaluated and compared between the groups using OCT.
- ***Result:*** A total of 77.4% of eyes with visual acuity of 6/60 or worse were in Group 1, showing a significant association. Bilateral cystoid macular edema was present in 80.8% of patients in Group 1, also statistically significant. The mean CMT was higher in Group 1 (330.96 ± 133.79 µm) compared to Group 2 (284.03 ± 93.26 µm), with a significant difference ($p = 0.001$).
- ***Conclusions:*** Ischemic heart disease is significantly associated with greater severity of diabetic macular edema, as evidenced by poorer visual acuity and more pronounced OCT findings. These results highlight the potential impact of systemic vascular conditions on ocular complications in diabetic patients.

- **Keywords:** Ischemic heart disease, macular edema, diabetes

INTRODUCTION

Diabetic maculopathy (DM) remains a leading cause of visual impairment in patients with diabetes mellitus. Traditional diagnostic tools such as fundus ophthalmoscopy and fluorescein angiography have been instrumental in clinical practice; however, they offer limited insight into the structural details of the retina. The advent of optical coherence tomography (OCT) has revolutionized retinal imaging by enabling high-resolution cross-sectional visualization of retinal layers. This advancement allows for accurate assessment of macular thickening, quantification of diabetic macular edema (DME), and detection of vitreoretinal traction (1).

DME can manifest at any stage of diabetic retinopathy and is a primary contributor to moderate vision loss in working-age adults (2). While macrovascular complications like myocardial infarction (MI) are well-documented in diabetes mellitus, microvascular complications such as DME also reflect the systemic impact of poor glycemic control and disease progression (3).

An understanding of macular anatomy is critical to appreciating the pathophysiology of diabetic maculopathy. The macula is a pigmented, oval-shaped area near the center of the retina, approximately 5.5 mm in diameter. It encompasses several regions including the umbo, foveola, foveal avascular zone, fovea, parafovea, and perifovea. Notably, the anatomical macula is larger than the clinically defined macula, which corresponds to the fovea at about 1.5 mm in diameter (4).

Diabetic maculopathy is defined by retinal thickening within one or two disc diameters of the macula. Edema results from fluid accumulation at the posterior pole, threatening vision when the central macula is involved. Although the precise mechanisms leading to maculopathy are not fully understood, increased capillary permeability and microcirculatory abnormalities are implicated. Poor metabolic control is believed to induce hemodynamic changes in retinal circulation, contributing to the pathogenesis of maculopathy (5).

Cystoid macular edema (CME), a severe manifestation of DME, is characterized by fluid accumulation within the intracellular spaces of the retina, primarily in the outer plexiform layer. The American Academy of Ophthalmology defines CME as macular thickening caused by disruption of the blood-retinal barrier, leading to perifoveal capillary leakage. This results in retinal distortion and photoreceptor dysfunction, which underlie visual impairment. CME is among the most common causes of central vision loss in the developed world (6).

The pathophysiological mechanisms of DME involve multiple metabolic disturbances including chronic hyperglycemia, dyslipidemia, oxidative stress, advanced glycation endproducts, and protein kinase C activation (7). Elevated levels of vascular endothelial growth factor (VEGF) play a key role in the breakdown of the inner blood–retinal barrier, promoting vascular leakage and retinal swelling (8).

OCT has become the cornerstone in the evaluation and classification of DME. This non-invasive imaging modality not only improves diagnostic accuracy but also serves as a reliable tool to monitor treatment response. With continued advancements, OCT is anticipated to remain the gold standard for diagnosing and following patients with macular edema (9).

From a systemic perspective, diabetes mellitus significantly increases the risk of ischemic heart disease (IHD), with affected patients experiencing higher rates of myocardial infarction. Although the exact pathogenesis remains complex, the prothrombotic and procoagulant state observed in diabetic individuals—characterized by increased glycoprotein IIB/IIIA receptors, elevated von Willebrand factor, and higher levels of plasminogen activator inhibitor type I—appears to promote thrombus formation and accelerate atherosclerosis. Additionally, proteinuria-related reductions in natural anticoagulants like protein C and antithrombin III further exacerbate this risk (10, 11).

Several clinical factors such as hypertension, diabetic nephropathy, and elevated glycated hemoglobin (HbA1c) have been identified as common risk factors for both DME and cardiovascular events (12). A recent retrospective study demonstrated that patients with DME experienced significantly more cardiovascular events—including myocardial infarction and cerebrovascular accidents—compared to diabetic individuals without retinal involvement (13). This suggests that retinal microvascular abnormalities might serve as early indicators of subclinical coronary or cerebral vascular disease, predisposing individuals to future cardiovascular events (14).

PATIENT and METHOD

This retrospective cohort study was conducted at the Medical City Complex—specifically in Ghazi Al-Hariri Teaching Hospital—in coordination with the Diabetic Disease Center at Baghdad Teaching Hospital. The study period extended from November 2018 to April 2019 and included a total of 128 patients (128 eyes), who were divided into two equal groups of 64 patients each.

The first group consisted of patients diagnosed with type 2 diabetes mellitus (non-insulin-dependent diabetes mellitus, NIDDM) for a duration between 5 to 15 years and with a confirmed history of ischemic heart disease (IHD). Diagnosis of IHD was based on either previous admission to a coronary care unit (CCU), cardiologist reports confirming ischemic events, or documented ECG findings. The second group included patients with type 2 diabetes mellitus for the same duration (5–15 years) but without any history of ischemic heart disease.

Each participant underwent a comprehensive interview and clinical assessment, including documentation of diabetes type and duration, number of ischemic events, previous ocular history (e.g., surgeries or anti-VEGF injections), and any factors that might affect ocular imaging. Visual acuity was assessed using the Snellen chart and slit-lamp biomicroscopy was performed to evaluate media clarity. All participants subsequently underwent macular evaluation using optical coherence tomography (OCT) to detect cystoid changes and measure central macular thickness (CMT).

Patients were included if they were over 50 years of age and had type 2 diabetes mellitus for 5 to 15 years. Exclusion criteria included patients with type 1 diabetes, uncertain or out-of-range diabetes duration, age below 50, severe systemic diabetic complications (e.g., diabetic foot or nephropathy), any media opacity affecting OCT interpretation or visual acuity, history of ocular surgery or anti-VEGF injections, and presence of non-diabetic retinal disease.

OCT imaging was performed at the Ophthalmology Department of Ghazi Al-Hariri Hospital using the same Optovue time-domain OCT device (software version 6.8.0.27) for all patients. The imaging was carried out by a consistent team of experienced optometrists. Pupillary dilation was performed when necessary to optimize image quality. Patients were instructed on proper fixation techniques to minimize motion artifacts. For this study, a CMT value of 275 µm was considered the upper normal limit, based on literature indicating that normal CMT rarely exceeds 253 µm. Changes exceeding 10% of baseline measurements were regarded as clinically significant, and cystoid macular edema (CME) was defined by the presence of cystic spaces in the macular region as seen on OCT.

Visual acuity was classified as follows: 6/6 was considered normal, 6/9 to 6/18 as mild visual impairment, 6/24 to 6/60 as moderate impairment, and 6/60 or worse as severe visual impairment.

Statistical analysis was performed using SPSS version 25. Data were presented as means, standard deviations, and ranges. The Chi-square test was used to determine associations between categorical variables, with a p-value of <0.05 considered statistically significant.

The study protocol received approval from the Iraqi Committee for Medical Specialization. All patients were informed about the nature and purpose of the study, and verbal consent was obtained prior to participation.

RESULTS

A total of 128 patients (256 eyes) diagnosed with type 2 diabetes mellitus were enrolled in this study. Participants were equally divided into two groups: Group 1 included 64 patients (128 eyes) with a documented history of ischemic heart disease (IHD), while Group 2 included 64 patients (128 eyes) without any history of IHD.

The patients' ages ranged from 50 to 81 years, with a mean age of 58.17 ± 7.6 years. Most participants (64.8%) were younger than 60 years. Overall, males accounted for a slightly higher proportion of the sample (54.7%) compared to females (45.3%), with a male-to-female ratio of 1.2:1.

In Group 1, the mean age was 59.23 ± 7.99 years, while in Group 2, the mean age was slightly lower at 56.99 ± 6.94 years. Regarding gender distribution, 31 male patients were in Group 1 (48.4% of group), compared to 39 in Group 2 (60.9%). Conversely, 33 female patients were in Group 1 (51.6%), and 25 in Group 2 (39.1%). Statistical analysis revealed no significant differences in age or gender distribution between the two groups ($P \geq 0.05$) **(Table 1).**

Table 1. Comparison between study groups in age.

Variable (n=128)	**First Group**	**Second Group**	**P - Value**
Age (Years) (Mean ± SD)	59.23 ± 7.99	56.99 ± 6.94	0.093
Gender			
Male	31 (48.4)	39 (60.9)	0.155
Female	33 (51.6)	25 (39.1)	

Of the 256 eyes evaluated, 46 eyes (18%) had normal visual acuity (VA). Among them, 16 eyes belonged to Group 1 (12.5%) and 30 eyes to Group 2 (23.4%).

Mild visual impairment was observed in 133 eyes (52%), with 63 eyes (49.2%) from Group 1 and 70 eyes (54.7%) from Group 2.

Moderate impairment was found in 46 eyes (18%), including 25 eyes from Group 1 (19.5%) and 21 eyes from Group 2 (16.4%).

Severe visual impairment was noted in 31 eyes (12%), with 24 eyes (18.8%) from Group 1 and only 7 eyes (5.5%) from Group 2, indicating a higher burden of severe vision loss among patients with IHD.

Out of 256 eyes, 143 (55.9%) had a Central Macular Thickness (CMT) of less than 275 µm—66 from Group 1 and 77 from Group 2. In contrast, 113 eyes (44.1%) had a CMT ≥275 µm—62 from Group 1 and 51 from Group 2—suggesting a greater prevalence of macular thickening among patients with IHD (Table 2).

Table 2. Distribution of study patients' eyes by clinical information

Clinical Parameters	**First Group n = 128**	**Second Group n = 128**	**Total (%) n = 256**
Visual Acuity			
Normal vision	16 (12.5)	30 (23.4)	46 (18.0)
Mild impairment	63 (49.2)	70 (54.7)	133 (52.0)
Moderate impairment	25 (19.5)	21 (16.4)	46 (18.0)
Severe impairment	24 (18.8)	7 (5.5)	31 (12.0)
Central Macular Thickness (µm)			
< 275	66 (51.6)	77 (60.2)	143 (55.9)
≥ 275	62 (48.4)	51 (39.8)	113 (44.1)

A significant relationship was observed between ischemic heart disease and visual acuity. Of the eyes with severe visual impairment, 77.4% belonged to patients with a history of IHD, compared to only 22.6% in the non-IHD group. Conversely, 65.2% of eyes with normal vision had no history of IHD (Table 3).

Table 3. Association between IHD and visual acuity

Variable	First Group n = 128	Second Group n = 128	Total (%) n = 256	P - Value
Visual Acuity				
Normal vision	16 (34.8)	30 (65.2)	46 (18.0)	**0.003**
Mild impairment	63 (47.4)	70 (52.6)	133 (52.0)	
Moderate impairment	25 (54.3)	21 (45.7)	46 (18.0)	
Severe impairment	24 (77.4)	7 (22.6)	31 (12.0)	

Among all 128 patients, 70 (54.7%) had normal Optical Coherence Tomography (OCT) findings. Of these, 26 were from Group 1 and 44 from Group 2. Unilateral cystoid macular edema (CME) was found in 32 patients (25%): 17 from Group 1 and 15 from Group 2. Bilateral CME was observed in 26 patients (20.3%), predominantly in Group 1 (21 patients), compared to only 5 patients in Group 2 (Table 4).

Table 4. Distribution of study patients by clinical information

Clinical Parameters	First Group n = 64	Second Group n = 64	Total (%) n = 128
Optical Coherence Tomography			
Unilateral Cystoid Macular Edema	17 (26.6)	15 (23.4)	32 (25.0)
Bilateral Cystoid Macular Edema	21 (32.8)	5 (7.8)	26 (20.3)
Normal	26 (40.6)	44 (68.8)	70 (54.7)
Number of ischemic attacks			
One	33 (51.6)	0 (0)	33 (51.6)
Frequent	31 (48.4)	0 (0)	31 (48.4)

In terms of OCT findings, bilateral CME was significantly more common in patients with IHD (80.8%) than those without (19.2%). Additionally, 62.9% of patients with normal OCT results had no history of IHD, compared to 37.1% with previous ischemic episodes (Table 5).

Table 5. Association between IHD and optical coherence tomography results

Variable	**First Group n = 64**	**Second Group n = 64**	**Total (%) n = 128**	**P - Value**
Optical Coherence Tomography Results				
Unilateral CME	17 (53.1)	15 (46.9)	32 (25.0)	**0.001**
Bilateral CME	21 (80.8)	5 (19.2)	26 (20.3)	
Normal	26 (37.1)	44 (62.9)	70 (54.7)	

Regarding central macular thickness, the mean CMT in Group 1 was significantly higher at 330.96 µm compared to 284.03 µm in Group 2 ($p < 0.05$), indicating more severe macular involvement in patients with IHD (Table 6).

Table 6. Comparison between study groups by CMT.

Central Macular Thickness (µm)	**First Group Mean ± SD**	**Second Group Mean ± SD**	**P - Value**
	330.96 ± 133.79	284.03 ± 93.26	**0.001**

Within Group 1, 33 patients had experienced a single ischemic event, while 31 had multiple events. Of the 26 patients with normal OCT findings, 12 had a single ischemic attack and 14 had multiple. Among the 17 patients with unilateral CME, 8 had one ischemic event and 9 had recurrent episodes. For the 21 patients with bilateral CME, 13 had experienced one ischemic attack, while 8 had multiple attacks.

Regarding gender-specific findings within Group 1 (31 males and 33 females): normal OCT findings were observed in 11 males and 15 females; unilateral CME in 7 males and 10 females; and bilateral CME in 13 males and 8 females (Table 7).

Table 7. Association between OCT and number of previous ischemic attacks

Variable	Optical Coherence Tomography Results			Total (%) n = 64	P - Value
	Bilateral CME n = 21	Unilateral CME n = 17	Normal n = 26		
No. of ischemic attacks					
One	13 (39.4)	8 (24.2)	12 (36.4)	33 (51.6)	0.511
Frequent	8 (25.8)	9 (29.0)	14 (45.2)	31 (48.4)	
Gender					
Male	13 (41.9)	7 (22.6)	11 (35.5)	31 (48.4)	0.320
Female	8 (24.2)	10 (30.3)	15 (45.5)	33 (51.6)	

DISCUSSION

In this study, there was no statistically significant difference between the two groups in terms of age or gender distribution ($p \geq 0.05$), indicating that these demographic variables were well-matched and unlikely to confound the results (Tables 1).

Regarding visual acuity, most eyes in both groups demonstrated mild visual impairment, with proportions of 49.2% and 54.7% in the first and second groups, respectively. However, normal visual acuity was more frequently observed in the second group, while the majority of eyes with severe visual impairment were found in the first group. Notably, 77.4% of eyes with severe visual loss had a history of ischemic heart disease, demonstrating a statistically significant association between visual acuity impairment and IHD ($p = 0.003$). These findings are consistent with previous work by St. Vincent et al., who reported a 30% reduction in visual acuity among patients with both type 2 diabetes and ischemic heart disease, attributing this to elevated serum triglyceride levels (19, 20).

In terms of central macular thickness (CMT), the first group showed a significantly higher mean value compared to the second group ($p = 0.001$), as detailed in Table 6. This result aligns with existing literature, such as a study that demonstrated a correlation between ischemic coronary artery disease and slight increases in retinal thickness and foveal volume (21).

Analysis of optical coherence tomography (OCT) findings revealed that a higher proportion of patients in the second group had normal OCT results, while bilateral cystoid macular edema (CME) was predominantly observed in the first group, accounting for 32.8% compared to only 7.8% in the second group. There was no significant difference between the groups regarding unilateral CME. However, bilateral CME showed a significant association with previous ischemic attacks, with 80.8% of such cases occurring in patients with IHD ($p = 0.001$). These observations are in agreement with earlier studies linking exudative diabetic maculopathy with ischemic heart disease due to dysregulated lipid profiles (22, 23). One comparative study noted that diabetic patients with severe exudative maculopathy had significantly higher serum triglyceride levels and a higher incidence of IHD than those with non-exudative retinopathy, although cholesterol levels did not differ significantly between the groups (22). In contrast, studies on type 1 diabetes have shown cholesterol elevations in association with exudative maculopathy, a finding not typically observed in type 2 diabetes (23, 24).

Further research has suggested that low-density lipoprotein (LDL) cholesterol may contribute to the development of diabetic maculopathy. Although conducted on small sample sizes, some studies have demonstrated a toxic effect of LDL on retinal capillary pericytes, particularly when LDL is glycated or oxidized (25, 26). Other investigations have identified lipoprotein (a) as a possible risk factor for maculopathy, though these findings remain preliminary due to limited patient numbers (27, 28). However, this interpretation contrasts with an earlier study by Ossama et al., which concluded that, after adjusting for confounding risk factors, the relationship between IHD and maculopathy lost statistical significance (29).

Additionally, no significant association was found between the number of ischemic heart disease attacks and OCT findings ($p = 0.511$), nor between OCT results and gender ($p = 0.320$), as shown in Table 7. These findings suggest that while IHD may influence the severity of macular pathology, the frequency of ischemic episodes or patient gender may not independently affect OCT outcomes in this context.

This study had several limitations that should be considered when interpreting the results. First, there was a lack of comparable data in the existing literature, as most studies did not include all of the parameters evaluated in our research, making direct comparisons challenging. Second, the study relied heavily on patient-reported history, particularly regarding the onset sequence of type 2 diabetes mellitus and ischemic heart disease, which introduces the potential for recall bias.

Accurately determining the duration of diabetes was also difficult in many cases, further limiting the precision of our findings. Additionally, the study population was restricted to a relatively narrow age range, which may limit the generalizability of the results to younger or significantly older individuals.

Logistical issues also posed challenges, particularly in patient referrals. The diabetic center and the ophthalmology department performing the OCT scans were located in separate hospitals, which may have affected the consistency and timeliness of evaluations. Furthermore, the classification of patients as having ischemic heart disease was largely dependent on the clinical judgment and documentation provided by other specialists, which could introduce variability in diagnosis.

Lastly, many patients in both groups had received antihypertensive medications due to episodic elevations in blood pressure, though they were not formally diagnosed with hypertension. This lack of clarity regarding blood pressure status may have influenced vascular findings, adding an additional confounding factor.

CONCLUSION

This study demonstrates a clear association between ischemic heart disease (IHD) and more severe diabetic macular involvement in patients with type 2 diabetes mellitus. Patients with IHD showed a higher incidence of severe visual acuity loss (≤6/60) and significantly greater central macular thickness, indicating more extensive retinal edema.

Bilateral cystoid macular edema (CME) was also more common in the IHD group, while unilateral CME showed no significant difference between groups. The number of ischemic heart attacks did not correlate with CME severity, suggesting that the presence of IHD itself may be more influential than the frequency of ischemic episodes.

RECOMMENDATIONS

Future studies should include all age groups and patients with type 1 diabetes to improve result applicability. Hypertension should be added as a variable due to its frequent coexistence with diabetes and ischemic heart disease. Research using fluorescein angiography is recommended to assess the impact of ischemic heart disease on ischemic maculopathy, especially in cases less responsive to anti-VEGF therapy. Further investigations are also needed to explore whether diabetic macular edema could be a risk factor for developing ischemic heart disease, highlighting the need for closer cardiac follow-up. Long-term studies are essential to better understand the relationship between atherosclerosis and diabetic retinopathy.

Ethical Clearance:

In accordance with the 2013 WMA Helsinki Declaration, all ethical aspects of this study were approved. Before enrolling the participants, an informed oral consent was obtained from their families as an ethical agreement. Additionally, approval from the hospital administrator was obtained.

Financial support and sponsorship:
Nil.
Conflicts of interest:
There are no conflicts of interest.

References

1. Sikorski BL, Malukiewicz G, Stafiej J, Lesiewska-Junk H, Raczynska D. The diagnostic function of OCT in diabetic maculopathy. Mediators Inflamm. 2013;2013:434560.
2. Nguyen-Khoa BA, Goehring EL, Werther W, Fung AE, Do DV, Apte RS, et al. Hospitalized cardiovascular events in patients with diabetic macular edema. BMC Ophthalmol. 2012;12:11.
3. Camici PG, Crea F. Coronary microvascular dysfunction. N Engl J Med. 2007;356(8):830–40.
4. Yanoff M. Ocular Pathology. 6th ed. Elsevier Health Sciences; 2009.
5. Zander E, Herfurth S, Bohl B, Heinke P, Herrmann U, Kohnert KD, et al. Maculopathy in patients with diabetes mellitus type 1 and type 2: associations with risk factors. Br J Ophthalmol. 2000;84(8):871–6.
6. Hogan P, Dall T, Nikolov P. Economic costs of diabetes in the US in 2002. Diabetes Care. 2003;26(3):917–32.
7. Bhagat N, Grigorian RA, Tutela A, Zarbin MA. Diabetic macular edema: pathogenesis and treatment. Surv Ophthalmol. 2009;54(1):1–32.
8. Zhang X, Bao S, Lai D, Rapkins RW, Gillies MC. Intravitreal triamcinolone acetonide inhibits breakdown of the blood-retinal barrier through differential regulation of VEGF-A and its receptors in early diabetic rat retinas. Diabetes. 2008;57(4):1026–33.
9. Romero-Aroca P. Managing diabetic macular edema: the leading cause of diabetes blindness. World J Diabetes. 2011;2(6):98–104.
10. Low Wang CC, Hess CN, Hiatt WR, Goldfine AB. Clinical update: cardiovascular disease in diabetes mellitus. Circulation. 2016;133(24):2459–502.
11. Leon BM, Maddox TM. Diabetes and cardiovascular disease: epidemiology, biological mechanisms, treatment recommendations and future research. World J Diabetes. 2015;6(13):1246–58.
12. Klein R, Knudtson MD, Lee KE, Gangnon R, Klein BE. The Wisconsin Epidemiologic Study of Diabetic Retinopathy XXIII: the twenty-five-year incidence

of macular edema in persons with type 1 diabetes. Ophthalmology. 2009;116(3):497–503.

13. Nguyen-Khoa BA, Goehring EL, Werther W, Fung AE, Do DV, Apte RS, et al. Hospitalized cardiovascular events in patients with diabetic macular edema. BMC Ophthalmol. 2012;12(1):11.
14. Kawasaki R, Cheung N, Islam FM, Klein R, Klein BE, Cotch MF, et al. Is diabetic retinopathy related to subclinical cardiovascular disease? Ophthalmology. 2011;118(5):860–5.
15. Chan A, Duker JS, Ko TH, Fujimoto JG, Schuman JS. Normal macular thickness measurements in healthy eyes using Stratus optical coherence tomography. Arch Ophthalmol. 2006;124(2):193–8.
16. Diabetic Retinopathy Clinical Research Network. Relationship between optical coherence tomography–measured central retinal thickness and visual acuity in diabetic macular edema. Ophthalmology. 2007;114(3):525–36.
17. Klein R, Klein BE, Moss SE. Visual impairment in diabetes. Ophthalmology. 1984;91(1):1–9.
18. Maberley DA, Hollands H, Chang A, Adilman S, Chakraborti B, Kliever G. The prevalence of low vision and blindness in a Canadian inner city. Eye (Lond). 2007;21(4):528–33.
19. Wood D, Durrington P, Poulter N, McInnes G, Rees A, Wray R. Joint British recommendations on prevention of coronary heart disease in clinical practice. Heart. 1998;80(Suppl 2):S1–29.
20. St Vincent Study Group. Diabetes care and research in Europe: the St Vincent Declaration. Diabet Med. 1990;7:360.
21. Gołebiewska J, Kęcik D, Turczyńska M, Moneta-Wielgoś J, Kopacz D, Pihowicz-Bakoń K. Evaluation of macular thickness after uneventful phacoemulsification in selected patient populations using optical coherence tomography. Klin Oczna. 2014;116(4).
22. Esmann V, Lundbaek K, Madsen PH. Types of exudates in diabetic retinopathy. Acta Med Scand. 1963;174:375–84.
23. Brown GC, Ridley M, Haas D, Lucier AC, Sarin LK. Lipaemic diabetic retinopathy. Ophthalmology. 1984;91:1490–5.
24. Dodson PM, Gibson JM. Long-term follow-up and underlying medical conditions in patients with diabetic exudative maculopathy. Eye. 1991;5:699–703.
25. Miccoli R, Odello G, Giampietro O, Marchetti P, Cristofani R, Penno G, et al. Circulating lipid levels and severity of diabetic retinopathy in type 1 diabetes mellitus. Ophthalmic Res. 1987;19:52–6.

26. Mohan R, Mohan V, Susheela L, Ramachandran A, Viswanathan M. Increased LDL cholesterol in non-insulin dependent diabetics with maculopathy. Acta Diabetol Lat. 1984;21:85–9.
27. Dornan TL, Carter RD, Bron AJ, Turner RC, Mann JI. Low-density lipoprotein cholesterol: an association with the severity of diabetic retinopathy. Diabetologia. 1982;22:167–70.
28. Guerci B, Meyer L, Sommer S, George JL, Ziegler O, Drouin P, et al. Severity of diabetic retinopathy is linked to lipoprotein (a) in type 1 diabetes. Diabetes Metab. 1999;25.
29. Klein R, Klein BE, Moss SE, Davis MD, DeMets DL. The Wisconsin epidemiologic study of diabetic retinopathy. Arch Ophthalmol. 1984;102(4):527–32.
30. Klein R, Klein BE, Moss SE. The epidemiology of proliferative diabetic retinopathy. Diabetes Care. 1992;15:1875–91.
31. Klein R, Klein BE, Moss SE, et al. Association of ocular disease and mortality in a diabetic population. Arch Ophthalmol. 1999;117:1487–95.