



Association of Steatotic Liver Disease with Retinal Vascular Occlusion: The Influence of Obesity in a Large Health Screening Cohort

Younjin Oh¹, Su Jeong Song²

¹College of Nursing, Yonsei University; ²Department of Ophthalmology, Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine, Seoul, Korea

In this cross-sectional study, we aimed to investigate the relationship between steatotic liver disease (SLD) and retinal abnormalities in a cohort undergoing health screening. Our study included 353,607 participants who underwent fundus photography and abdominal ultrasonography at least once at the Kangbuk Samsung Health Promotion Center from 2002 to 2022. After adjusting for age and sex, the risk of retinal vein occlusion (RVO) significantly increased with the presence of non-alcoholic fatty liver disease, metabolic dysfunction-associated fatty liver disease, and metabolic dysfunction-associated SLD, with odds ratios of 1.259 (95% confidence interval [CI], 1.050 to 1.510), 1.498 (95% CI, 1.249 to 1.796), and 1.342 (95% CI, 1.121 to 1.605), respectively. However, these associations weakened after adjusting for body mass index. No statistically significant associations were observed with other retinal disorders after adjusting for age, sex, and other confounding factors. Our findings suggest that obesity may mediate the relationship between SLD and RVO, while other retinal abnormalities may be more closely associated with known risk factors rather than SLD itself.

Keywords: Fatty liver; Retinal diseases; Diabetic retinopathy; Macular degeneration; Retinal vein occlusion; Obesity

INTRODUCTION

The retinal vasculature offers a unique, non-invasive view of human circulation, providing insights into how systemic and metabolic diseases affect microcirculation [1]. The term ‘steatotic liver disease’ (SLD) has recently been recommended as an umbrella term for excess liver fat [2]. The connection between SLD and vascular disease is thought to involve several mechanisms: chronic low-grade inflammation, oxidative stress, insulin resistance, dyslipidemia, and the accumulation of advanced glycation end-products. These factors, along with increased hepatic pro-

duction of procoagulant factors, may impair endothelial function, promote vascular stiffness and remodeling, and elevate thrombotic risk, thereby contributing to systemic and retinal vascular dysfunction [3-7]. Historically, ‘non-alcoholic fatty liver disease’ (NAFLD) was the term used to describe increased hepatic fat accumulation not related to alcohol consumption. This term has since evolved to include ‘metabolic dysfunction-associated fatty liver disease’ (MAFLD) and more recently, ‘metabolic dysfunction-associated steatotic liver disease’ (MASLD) [2,8,9]. Furthermore, the term ‘metabolic dysfunction-associated steatotic liver disease with increased alcoholic intake’ (MetALD)

Received: 21 September 2024, **Revised:** 29 October 2024,
Accepted: 17 November 2024

Corresponding author: Su Jeong Song
Department of Ophthalmology, Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine, 29 Saemunan-ro, Jongno-gu, Seoul 03181, Korea
Tel: +82-2-2001-2250, **Fax:** +82-2-2001-2486, **E-mail:** sjsong7@gmail.com

Copyright © 2025 Korean Endocrine Society

This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (<https://creativecommons.org/licenses/by-nc/4.0/>) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

has been proposed to describe MASLD with concurrent excessive alcohol intake, reflecting the evolving understanding of the interplay between fatty liver disease, metabolic health, and alcohol consumption [2].

While several studies have described the link between retinal abnormalities and metabolic diseases, there is limited research on their relationship with the newly recommended classifications of metabolic dysfunction-associated SLDs. Therefore, we aimed to investigate the potential link between retinal abnormalities and the updated classifications of SLDs, with a special focus on metabolic dysfunction.

METHODS

In this cross-sectional study, we examined the relationship between SLD and retinal abnormalities in a large Korean cohort of 353,607 participants, aged 20 years or older, who underwent at least one health examination, including abdominal ultrasonography and fundus photography, from 2002 to 2022 at the Kang-

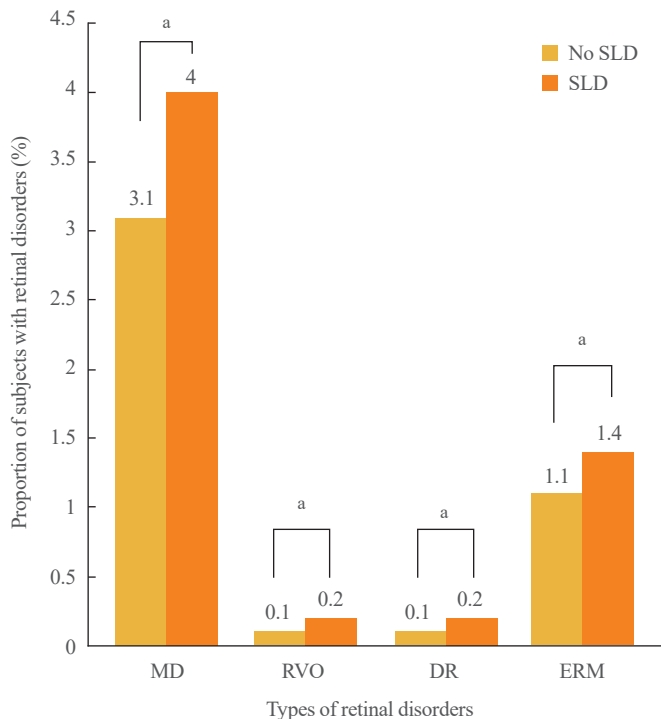


Fig. 1. Prevalence of retinal disorders according to the presence and absence of steatotic liver disease (SLD). The prevalence was significantly higher in participants with SLD than in those without SLD with macular degeneration (MD) showing the largest difference. RVO, retinal vein occlusion; DR, diabetic retinopathy; ERM, epiretinal membrane. ^a $P < 0.01$ between SLD and no SLD groups by chi-square test.

buk Samsung Health Promotion Center.

Abdominal ultrasonography was conducted by experienced radiologists who were blinded to the study objectives. Fatty liver was diagnosed based on standard criteria: a diffuse increase in fine echoes in the liver parenchyma compared to those in the kidney or spleen parenchyma, deep beam attenuation, and bright vessel walls. The diagnosis of fatty liver showed substantial interobserver reliability (kappa statistic=0.74) and excellent intraobserver reliability (kappa statistic=0.94) [10]. The presence of SLD was defined according to established criteria for NAFLD, MAFLD, MASLD, and MetALD [2,8,9].

Ophthalmic examinations utilized nonmydriatic fundus cameras, and retinal abnormalities were classified according to international standards. Macular degeneration (MD) was identified in both its early and late stages; diabetic retinopathy (DR) included any signs, irrespective of severity; retinal vein occlusion (RVO) encompassed all features, including historical cases; and epiretinal membrane (ERM) covered conditions such as cellophane macular reflex and preretinal macular fibrosis.

Prevalence was compared between the SLD and non-SLD groups using the chi-square test. Continuous variables were assessed for normality through graphical methods. Variables that were normally distributed are presented as the mean $\pm$ standard deviation and were compared using the Student *t* test. In contrast, variables that were not normally distributed are presented as the median and were compared using the Mann-Whitney *U* test. Odds ratios (ORs) for retinal disorders based on SLD status were calculated using multinomial logistic regression models, with adjustments for age, sex, body mass index (BMI), diabetes status, and other confounders. Statistical analyses were conducted using SPSS version 19.0 (IBM Corp., Armonk, NY, USA), and *P* values less than 0.05 were considered statistically significant.

This study received approval from the Institutional Review Board of Kangbuk Samsung Hospital (KBSMC 2024-05-047). The need for informed consent was waived because the study utilized de-identified retrospective data.

RESULTS

Baseline characteristics of the participants

The mean age of the study participants was 42 years, with men comprising 49.7% of the sample (Supplemental Table S1). The overall prevalence of SLD stood at 29.1%, with the breakdown as follows: NAFLD at 26.2%, MAFLD at 23.4%, MASLD at 27.9%, and MetALD at 2.3%. Regarding retinal abnormalities, 7.6% of the participants exhibited some form of abnormality.

The most common was MD, affecting 3.4% of the sample, followed by ERM at 1.2%, and both RVO and DR at 0.1% each (Supplemental Table S1).

Participants with SLD were significantly older, had higher BMIs, and exhibited worse metabolic profiles, characterized by elevated blood pressure, fasting glucose, and abnormal lipid levels. Retinal abnormalities were more prevalent in those with SLD compared to those without (9.2% vs. 7.0%, $P < 0.01$). The prevalence of all retinal disorders was significantly higher in the SLD group (Fig. 1).

Risks of retinal disorders by SLD status

After adjusting for age and sex, the risk of RVO was significantly higher in participants with NAFLD, MAFLD, and MASLD, with ORs of 1.259 (95% confidence interval [CI],

1.050 to 1.510), 1.498 (95% CI, 1.249 to 1.796), and 1.342 (95% CI, 1.121 to 1.605), respectively (Table 1). These associations were attenuated after further adjustment for BMI.

No significant associations were found between SLD and other retinal disorders such as MD, DR, and ERM, even after adjusting for confounding variables.

DISCUSSION

In this cross-sectional study of 353,607 participants undergoing health examinations, we discovered that the risk of RVO was significantly higher in individuals diagnosed with MAFLD and MASLD, which are recent terminological replacements for NAFLD. The associations persisted even after adjustments for age and sex. However, the significance was diminished when

Table 1. Risk of Retinal Disorders according to Steatotic Liver Disease Status

Variable	Odds ratio (95% confidence interval)			
	Model 1	Model 2	Model 3	Model 4
Macular degeneration ^a				
NAFLD	1.322 (1.272–1.374)	1.023 (0.982–1.065)	0.929 (0.887–0.973)	0.956 (0.912–1.002)
MAFLD	1.042 (0.999–1.087)	1.042 (0.999–1.087)	0.959 (0.911–1.010)	0.963 (0.915–1.014)
MASLD	1.322 (1.272–1.374)	1.023 (0.982–1.065)	0.951 (0.907–0.998)	0.955 (0.911–1.002)
MetALD	1.339 (1.204–1.490)	1.179 (1.058–1.315)	1.118 (1.001–1.249)	1.021 (0.910–1.146)
Retinal vascular occlusion ^b				
NAFLD	1.639 (1.369–1.962)	1.259 (1.050–1.510)	0.953 (0.782–1.161)	-
MAFLD	2.018 (1.688–2.412)	1.498 (1.249–1.796)	1.091 (0.886–1.344)	-
MASLD	1.752 (1.468–2.090)	1.342 (1.121–1.605)	0.991 (0.811–1.211)	-
MetALD	1.087 (0.626–1.886)	1.086 (0.623–1.896)	0.889 (0.508–1.554)	-
Diabetic retinopathy ^c				
NAFLD	2.493 (2.063–3.013)	1.829 (1.511–2.215)	1.631 (1.323–2.010)	0.891 (0.723–1.097)
MAFLD	3.148 (2.606–3.803)	2.209 (1.822–2.679)	2.089 (1.668–2.617)	0.810 (0.649–1.012)
MASLD	2.795 (2.313–3.376)	1.998 (1.648–2.422)	1.818 (1.464–2.258)	0.800 (0.643–0.996)
MetALD	1.820 (1.135–2.919)	1.431 (0.889–2.306)	1.242 (0.768–2.008)	0.762 (0.471–1.234)
Epiretinal membrane ^d				
NAFLD	1.297 (1.214–1.385)	1.033 (0.965–1.105)	-	-
MAFLD	1.320 (1.234–1.412)	1.023 (0.954–1.097)	-	-
MASLD	1.284 (1.204–1.370)	1.031 (0.964–1.102)	-	-
MetALD	0.872 (0.703–1.080)	0.995 (0.800–1.239)	-	-

NAFLD, non-alcoholic fatty liver disease; MAFLD, metabolic dysfunction-associated fatty liver disease; MASLD, metabolic dysfunction-associated steatotic liver disease; MetALD, metabolic dysfunction-associated steatotic liver disease with increased alcoholic intake.

^aModel 1 (crude model), model 2 (age and sex-adjusted), model 3 (model 2+body mass index, systolic blood pressure, diabetes mellitus, total cholesterol, homeostasis model assessment index-insulin resistance, and triglycerides), model 4 (model 3+amount of daily alcohol intake); ^bModel 1 (crude model), model 2 (age and sex-adjusted), model 3 (model 2+body mass index); ^cModel 1 (crude model); model 2 (age and sex-adjusted), model 3 (model 2+body mass index), model 4 (model 3+diabetes mellitus); ^dModel 1 (crude model), model 2 (age and sex-adjusted).

BMI was considered, indicating that obesity might play a central role in mediating the relationship between SLD and RVO. This observation is particularly significant as our research is among the first to propose that SLD could be a risk factor for RVO, with obesity possibly serving as a mediator. These results underscore the importance of considering potential confounding factors, such as obesity, when examining the relationship between SLD and RVO.

The observed relationship between SLD and RVO, which is potentially mediated by obesity, warrants further investigation. Obesity is a well-established risk factor for both SLD and various cardiovascular conditions. Additionally, RVO is often regarded as a manifestation of systemic vascular disease [11,12]. Although limited research directly linking SLD to RVO exists, some studies have explored the association between obesity and RVO. For example, a nationwide study in Korea involving over 23 million adults aged 20 years and older found a linear relationship between BMI and RVO risk in individuals without diabetes, a relationship that was reversed in those with diabetes [13]. Another study using the same population demonstrated that the presence of metabolic syndrome and its associated risk factors significantly increased the risk of RVO, highlighting the harmful effects of insulin resistance and obesity on RVO risk, which is consistent with our findings [14]. These results support the possibility that the link between SLD and RVO may reflect broader cardiovascular risks associated with metabolic dysfunction.

Our study has several limitations. First, its cross-sectional design limits the ability to generalize our findings to other populations and precludes the determination of causal relationships. Second, different models and adjustment factors were used for each regression analysis, which could weaken the overall significance of the results for the range of retinal disorders studied. However, since various retinal disorders arise from different pathophysiological mechanisms and are influenced by distinct risk factors, applying uniform adjustment factors was impractical. Lastly, cardiovascular risk factors such as blood pressure and specific lipid profiles were not independently adjusted for in the RVO analysis. These factors are known to be strongly associated with RVO and could potentially influence the observed associations. While adjusting for BMI addresses some aspects of metabolic health, it may not fully account for the independent effects of cardiovascular parameters. More rigorous prospective studies with detailed designs are needed to clarify the mechanistic links between SLD and RVO.

In conclusion, the findings of our study suggest that SLD may be associated with an increased risk of RVO, potentially medi-

ated by obesity. However, no significant associations were found between SLD and other retinal disorders after adjusting for relevant confounding factors. Further research is needed to elucidate the specific mechanisms linking obesity, SLD, and RVO, and to explore potential preventive strategies targeting these interconnected metabolic conditions.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

AUTHOR CONTRIBUTIONS

Conception or design: S.J.S. Acquisition, analysis, or interpretation of data: S.J.S. Drafting the work or revising: Y.O., S.J.S. Final approval of the manuscript: S.J.S.

ORCID

Younjin Oh <https://orcid.org/0009-0007-8398-8219>

Su Jeong Song <https://orcid.org/0000-0003-2110-1874>

REFERENCES

1. Nguyen TT, Wong TY. Retinal vascular manifestations of metabolic disorders. *Trends Endocrinol Metab* 2006;17:262-8.
2. Rinella ME, Lazarus JV, Ratziu V, Francque SM, Sanyal AJ, Kanwal F, et al. A multisociety Delphi consensus statement on new fatty liver disease nomenclature. *J Hepatol* 2023;79:1542-56.
3. Huang DQ, Downes M, Evans RM, Witztum JL, Glass CK, Loomba R. Shared mechanisms between cardiovascular disease and NAFLD. *Semin Liver Dis* 2022;42:455-64.
4. Rhee EJ. The influence of obesity and metabolic health on vascular health. *Endocrinol Metab (Seoul)* 2022;37:1-8.
5. Teo ZL, Tham YC, Yu M, Chee ML, Rim TH, Cheung N, et al. Global prevalence of diabetic retinopathy and projection of burden through 2045: systematic review and meta-analysis. *Ophthalmology* 2021;128:1580-91.
6. Zhu W, Wu Y, Meng YF, Xing Q, Tao JJ, Lu J. Association of obesity and risk of diabetic retinopathy in diabetes patients: a meta-analysis of prospective cohort studies. *Medicine (Baltimore)* 2018;97:e11807.
7. Mbata O, Abo El-Magd NF, El-Remessy AB. Obesity, metabolic syndrome and diabetic retinopathy: beyond hypergly-

- cemia. *World J Diabetes* 2017;8:317-29.
8. Pouwels S, Sakran N, Graham Y, Leal A, Pintar T, Yang W, et al. Non-alcoholic fatty liver disease (NAFLD): a review of pathophysiology, clinical management and effects of weight loss. *BMC Endocr Disord* 2022;22:63.
 9. Eslam M, Newsome PN, Sarin SK, Anstee QM, Targher G, Romero-Gomez M, et al. A new definition for metabolic dysfunction-associated fatty liver disease: an international expert consensus statement. *J Hepatol* 2020;73:202-9.
 10. Bird AC, Bressler NM, Bressler SB, Chisholm IH, Coscas G, Davis MD, et al. An international classification and grading system for age-related maculopathy and age-related macular degeneration. The International ARM Epidemiological Study Group. *Surv Ophthalmol* 1995;39:367-74.
 11. Piche ME, Tchernof A, Despres JP. Obesity phenotypes, diabetes, and cardiovascular diseases. *Circ Res* 2020;126:1477-500.
 12. Ip M, Hendrick A. Retinal vein occlusion review. *Asia Pac J Ophthalmol (Phila)* 2018;7:40-5.
 13. Paik DW, Han K, Kang SW, Ham DI, Kim SJ, Chung TY, et al. Differential effect of obesity on the incidence of retinal vein occlusion with and without diabetes: a Korean nationwide cohort study. *Sci Rep* 2020;10:10512.
 14. Lim DH, Shin KY, Han K, Kang SW, Ham DI, Kim SJ, et al. Differential effect of the metabolic syndrome on the incidence of retinal vein occlusion in the Korean population: a nationwide cohort study. *Transl Vis Sci Technol* 2020;9:15.