

OCTA-Derived Retinal Biomarkers for Cardiovascular Risk Stratification: A Narrative Review

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ABSTRACT

Optical Coherence Tomography Angiography (OCTA) is transforming the way we understand the connection between retinal health and cardiovascular disease (CVD). The retina, often considered a reflection of systemic vascular health, provides a non-invasive way to assess microvascular changes that may indicate early signs of cardiovascular issues. This review explores OCTA's potential in detecting subtle retinal alterations that could serve as biomarkers for CVD risk and early diagnosis.

To explore this, a comprehensive literature review was conducted, drawing from databases like PUBMED-MEDLINE, Scopus, and Google Scholar, covering studies from 2015 to 2024. Research focused on retinal vascular changes in individuals with CVD and how OCTA-derived parameters could serve as diagnostic indicators. The findings suggest that specific microvascular changes such as reduced vessel density, capillary dropout, and modifications in the foveal avascular zone are associated with systemic vascular dysfunction. These alterations are particularly linked to conditions like hypertension, diabetes, and atherosclerosis, reinforcing the idea that retinal imaging could be a valuable tool in cardiovascular risk assessment.

With its ability to provide high-resolution, real-time insights into retinal microvasculature, OCTA emerges as a promising tool in bridging ophthalmology and cardiology. As research continues to refine the role of retinal biomarkers in CVD detection, integrating OCTA into routine cardiovascular risk assessment could enhance early diagnosis and monitoring strategies. Standardization of OCTA-derived metrics will be key to making this technology a mainstream part of cardiovascular healthcare in the future.

KEYWORDS: Optical Coherence Tomography Angiography, Cardiovascular Disease, Foveal Avascular Zone, Artificial Intelligence, Machine Learning

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INTRODUCTION

The most common cause of cardiovascular disease (CVD) in the world is ischaemic heart disease with an age standardised mortality rate of 108.8 deaths per 100,000 people.[1] Additionally, hypertension is the leading CVD modifiable risk factor worldwide, with 10.8 million deaths due to the condition in 2019.[2] Because heart diseases are a major cause of mortality, their early detection and prevention is critical to enhancing patient outcomes.[3] Recent research has shown that retinal imaging provides a non-invasive modality to evaluate structural and functional features of the retinal vasculature, such as the microcirculation and vessel properties, thus giving information on the health of the arteries in the body.[4] Changes in the retinal vasculature have been linked with a systemic cardiovascular risk and disease; therefore, ophthalmic imaging has become a useful approach in assessing cardiovascular risk with retinal microvascular signs being promising biomarkers in the clinical environment.[5]

Various modalities are used in the primary diagnosis of vascular disorders. Traditional methods, like laboratory blood biomarkers, electrocardiography, and imaging methods that measure the arterial stiffness, usually detect disease at a rather late stage.[6] These techniques might not be able to identify the microvascular alterations that exist before clinical evidence. As a result, the non-invasive imaging modalities with high-resolution that can provide early information about the health of the systemic vessels are becoming increasingly popular.

Optical coherence tomography angiography (OCTA) is a non-invasive imaging modality that allows a complete analysis of ocular blood flow in the vascular arrangements of the eye.[7] OCTA can capture angiographic images of the ocular vascularity rapidly by repeatedly scanning a specific location on the retina.[8] Unlike the traditional imaging modalities, OCTA provides real-time visualisation of capillary networks without the use of contrast agents. It identifies changes in retinal arterial density, perfusion, and capillary dropout, which have been linked to a number of cardiovascular risk factors such as atherosclerosis, diabetes and hypertension. OCTA has the potential to become an important instrument of cardiovascular risk stratification and disease monitoring through the evaluation of microvascular integrity in a non-invasive way.

While multiple studies have explored retinal biomarkers in systemic diseases, a comprehensive synthesis of OCTA-derived parameters specifically linked to cardiovascular risk remains limited. This review aims to discuss how OCTA can detect retinal microvascular alterations related to cardiovascular disease and will provide an explanation of the clinical implications of OCTA in the early diagnosis of CVD and assess its possible role in cardiovascular risk assessment protocols.

UNDERSTANDING RETINAL MICROVASCULATURE AND SYSTEMIC HEALTH

A literature search was conducted in PubMed, Scopus, and Google Scholar for articles published from 2015 to 2024 utilising the keywords: “optical coherence tomography angiography,” “OCTA,” “retinal microvasculature,” and “cardiovascular disease.” Only human clinical trials and relevant review articles published in English were included.

2.1 Anatomy and Physiology of the Retinal Microvasculature

The retina is the most metabolically active tissue in the body, which requires the continuous and strictly controlled blood flow.[9] The retinal microvascular plexus has three key layers, namely: the superficial vascular plexus (SVP); the deep vascular plexus (DVP); and the choriocapillaris. The choriocapillaris, filled by the posterior ciliary arteries, is supplying the outer retina, the photoreceptor cells in particular, with oxygen and nutrients, and the SVP and DVP formed by the central retinal artery mostly supply the inner retinal layers. This dual circulation is the one that maintains the best performance of the retina and demonstrates the wellness of the systemic arteries.[10] Instead of autonomic innervation, retinal microvasculature relies on local autoregulatory processes to sustain blood flow; the vascular integrity and metabolic response of endothelial cells, pericytes, and astrocytes are important. Similar to the blood brain barrier, the blood retinal barrier (BRB) does not allow large molecules to pass through it, as this provides protection of the retina against systemic variations. However, systemic diseases including diabetes, high blood pressure and atherosclerosis may upset this delicate balance causing microvascular deformities that can be detected through retinal imaging.[11]

2.2 How Retinal Microcirculation Reflects Systemic Vascular Health

The retinal microvasculature is a useful indicator of systemic vascular health because it is structurally and functionally comparable to the cerebral and coronary microcirculation. Various cardiovascular diseases have been associated with changes in the retinal vessel calibre, tortuosity and capillary density. Retinal imaging allows direct evaluation of the microvasculature, which makes the condition of other organs like the heart to be reflected.[4] Just like other modalities, retinal imaging often demonstrates endothelial dysfunction and microvascular rarefaction (which are early signs of atherosclerosis before clinical signs of CVD become evident). Moreover, oxidative stress and inflammatory processes influence retinal microcirculation, both of which play a crucial role in the CVD pathophysiology. An early onset of endothelial dysfunction can be characterised by high levels of vascular permeability and capillary dropout in the retina, which allow the cardiovascular risk to be assessed in time. Monteiro-Henriques et al. (2021) summarized that OCTA consistently reveals reduced retinal and choroidal vessel density and enlarged foveal avascular zones in systemic cardiovascular diseases and risk factors, highlighting its potential as a non-invasive biomarker of cardiovascular risk. [12]

2.3 Overview of Key Microvascular Parameters Assessed by OCTA

OCTA has revolutionized the process of imaging retinal vasculature because it allows imaging microvascular networks in high detail without contrast dyes. Many of the critical indicators which are measured by OCTA show close relationships with cardiovascular health. Vessel density (VD) is one of them; lower vessel density in the retina has been associated with diseases of

the systemic vessels, such as diabetes and hypertension.[7] Foveal avascular zone (FAZ) expansion is another significant indicator that is usually seen in ischemic diseases like coronary artery disease and indicates the presence of microvascular dysfunction.[7] Also, OCTA shows that capillary perfusion and flow deficits can be early signs of microvascular damage in all types of metabolic and cardiovascular diseases.[7] The changes in retinal vascular tortuosity and fractal dimension, which reflect the alteration of the vessel branching patterns, may be informative on the atherosclerotic load and endothelial dysfunction on a systemic scale.[7] OCTA offers a quantitative, non-invasive approach to detecting early vascular abnormalities that may signal the presence of cardiovascular disease. With the evolution of the research, the incorporation of retinal microvascular measurements into the routine cardiovascular screening systems has the power to contribute to the increase of the early detection rates and the improvement of preventive measures.

OPTICAL COHERENCE TOMOGRAPHY ANGIOGRAPHY (OCTA): A NON-INVASIVE IMAGING TOOL

3.1 Principles and Technology Behind OCTA

Optical Coherence Tomography Angiography (OCTA) is a highly advanced, non-invasive imaging technique that provides high-resolution, depth-resolved visualization of the retinal and choroidal microvasculature. Unlike the traditional dye-based angiography, OCTA identifies the blood flow by analysing the motion contrast signals when red blood cells pass through the vessels of the vasculature.[7] It is achieved through the series of cross-sectional scans at a fixed point on the retina, where the changes in the intensity of backscattered light are used to create detailed vascular maps.[8]

Without the use of contrast chemicals, OCTA distinguishes between flowing blood and static tissue using the decorrelation signal processing approach. In contrast to previous imaging modalities, which produced only two dimensional images of retinal vasculature, OCTA can provide depth resolved *in vivo* imaging of the retinal microvasculature without the need to inject a dye into the retina.[13] OCTA imaging is used to map out retinal microvasculature in multiple layers in spectral-domain (SD-OCT) or swept swept-source (SS-OCT) technology helping with fast imaging on a micron-scale level.[14] This is made possible to provide unmatched information on the health of the vascularity including the choriocapillaris, outer retina and superficial and deep capillary plexus.

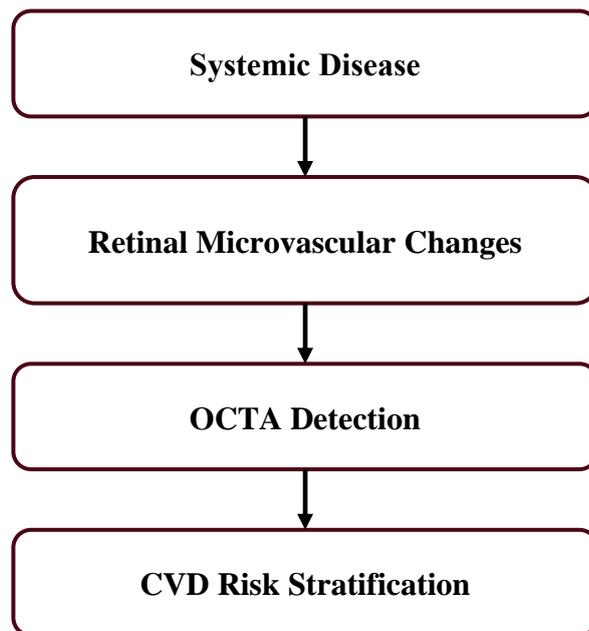


Figure 1. Flowchart illustrating the link between systemic vascular disease and retinal microvascular biomarkers detected by OCTA.

3.2 Advantages of OCTA Over Traditional Imaging Techniques

OCTA has a number of unique benefits compared to the other more accepted imaging modalities available, fundus photography, fluorescein angiography (FA), and indocyanine green angiography (ICGA). First, it is non-invasive and dye-free, which significantly increases its safety as compared to FA and ICGA, which involve the use of intravenous contrast agents, which have risks of allergic reactions or systemic side effects.[15] Second, OCTA allows visualization of retinal vasculature in layers, which allows visualization of depth resolved retinal vasculature and differentiation between superficial and deep capillary plexuses not possible with traditional FA.[15] Moreover, OCTA aids in high-speed and high-resolution imaging, which makes it a proper method of identifying subtle changes in micro vascularity by quickly obtaining images with adequate resolution to outline single capillaries.[15] The other advantageous feature is its quantitative analysis ability OCTA provides objective, quantifiable vascular features including vessel density, flow area and foveal avascular zone (FAZ) size that can be utilized to track disease progression with accuracy and precision.[15] All these properties make OCTA a revolutionary tool in the evaluation of systemic vascular diseases, especially cardiovascular disorders, besides its use in ocular health.

3.3 OCTA-Derived Biomarkers Relevant to Systemic Vascular Diseases

The current study suggests that biomarkers obtained through OCTA can be used as the predictors of cardiovascular disease since they provide essential data on systemic vascular dysfunction. Some of the relevant biomarkers are vascular tortuosity, fractal dimension, capillary non-perfusion, and flow deficits, choriocapillaris flow deficits, FAZ enlargement, and retinal vessel density (VD). Through the exploitation of these biomarkers, OCTA connects cardiology and ophthalmology by providing a powerful, non-invasive technique of assessing micro-vascular health. This imaging method has the potential to revolutionize early disease detection and cardiovascular risk determination as our understanding of the OCTA-based systemic biomarkers matures or improves with time.[7]

| OCTA Biomarker | Associated Systemic / Cardiovascular Condition | Typical OCTA Change Observed | Clinical Interpretation / Importance |
|----------------------------------------------|------------------------------------------------|------------------------------------------|--------------------------------------------------------------------------------|
| Vessel Density (VD) – SCP & DCP | Hypertension, CAD, Diabetes | ↓ Reduced VD | Indicates microvascular rarefaction and endothelial dysfunction |
| Foveal Avascular Zone (FAZ) Area | Diabetes, Smoking, Ischemic Heart Disease | ↑ Enlarged FAZ | Suggests ischemic microvascular remodeling |
| Perfusion Density (PD) | Coronary artery disease, Heart failure | ↓ PD | Reflects impaired retinal blood flow perfusion |
| Radial Peripapillary Capillary (RPC) Density | Hypertension, Dyslipidemia | ↓ RPC density | Suggests compromised optic nerve microcirculation |
| Choriocapillaris Flow Deficits | Atherosclerosis, Systemic inflammatory disease | ↑ Flow void areas | Indicates compromised choroidal circulation linked to systemic vascular status |
| Deep Vascular Plexus Vessel Tortuosity | Diabetes & Microangiopathy | ↑ Tortuosity & irregular vessel geometry | Early biomarker of metabolic and vascular damage |

Table 1. Summary of key OCTA-derived retinal biomarkers and their associations with systemic cardiovascular and metabolic conditions.

Main retinal vascular parameters that can be measured by Optical Coherence Tomography Angiography (OCTA) as shown in table 2. These include vessel density, foveal avascular zone area, perfusion density, radial peripapillary capillary density, choriocapillaris flow deficits, and vascular tortuosity. It also shows how these parameters usually change in systemic diseases like hypertension, diabetes, atherosclerosis, and dyslipidaemia. The clinical interpretation of each biomarker is clarified for cardiovascular risk stratification.

RETINAL MICROVASCULAR CHANGES IN CARDIOVASCULAR DISEASE

Optical Coherence Tomography Angiography (OCTA) helps to monitor overall microvascular health and its relationship to systemic diseases.

4.1 Hypertension and Its Retinal Microvascular Manifestations

Hypertension is a well-established cardiovascular risk factor of strong impact on the retinal microvasculature. OCTA has been found to be effective in identifying most of the anatomical and functional changes on retinal arteries caused by increased blood pressure. Arterial constriction and a decrease in vessel density is a hallmark characteristic of hypertensive patients, which develops as a result of long-term vasoconstriction caused by chronic hypertension. Hypertensive patients have always been observed to have reduced retinal vascular density especially in the superficial and deep capillary plexuses in the OCTA studies, which is also known as hypoxia due to the absence of oxygen in the blood of the retinal tissue and hemorrhagic strokes.[16] Besides, higher retinal vascular tortuosity is common with hypertension, where the compliance of vascular walls is compromised, leading to the abnormal vessel curvature, a fledgling sign of systemic vascular dysfunction.[16] Also, OCTA is able to detect ischemic changes and capillary non-perfusion, which reveal the areas of capillary drop-out and perfusion loss that indicate microvascular damage and can indicate an increased risk of end-organ complications such as stroke and heart disease in advance.[16] These results highlight the importance of OCTA in early identification of hypertensive microvascular damage and its possible role in screening and monitoring of the treatment outcomes in hypertensive individuals.

4.2 Diabetes-Related Microvascular Changes and CVD Risk

The diabetes mellitus is a familiar risk factor of both microvascular and macrovascular complications, such as diabetic retinopathy and cardiovascular disease. The retinal microvasculature change is one of the earliest signs of systemic endothelial dysfunction in diabetes and provides useful information on the overall state of arteries. One of the most noticeable alterations which can be identified by OCTA is capillary rarefaction and decreased vessel density particularly in the deep capillary plexus which is closely linked with increased risk of cardiovascular disease and more widespread microvascular dysfunction of the whole body.[17] FAZ enlargement, which is an indication of ischemic damage to the retinal microcirculation, is another typical observation in diabetic subjects, and is associated with increased cardiovascular morbidity.[17] Microaneurysms and capillary dropout are also early signs of vascular compromise in diabetes, which are endothelial dysfunction and vessel wall vulnerability indicators. OCTA is able to identify the deficit of choriocapillaris flow, which has been implicated in the evolution of diabetic retinopathy and the general systemic vascular impairment of the vascular system.[17] As diabetes is strongly linked with cardiovascular mortality,

OCTA-retinal image has a high potential, as it is a non-invasive method of early detection and longitudinal follow-up of systemic microvascular impairments in diabetic patients.

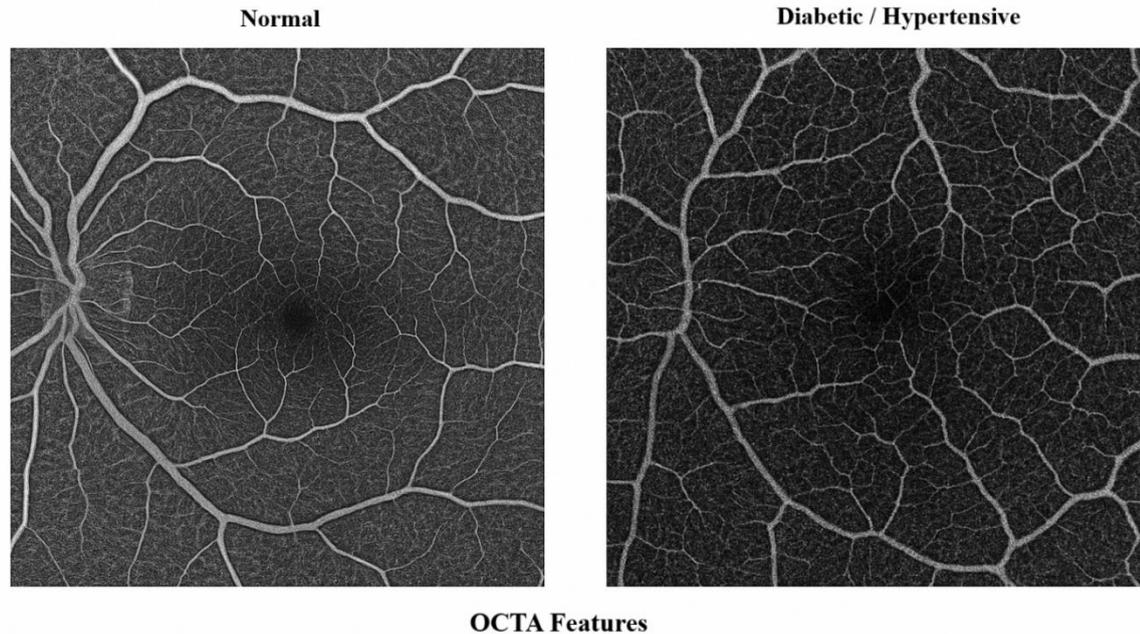


Figure 2. Optical Coherence Tomography Angiography (OCTA) comparison of a normal retinal microvascular network versus one affected by hypertension or diabetes. Notable differences include reduced vessel density and areas of capillary dropout in the diseased state.

4.3 Atherosclerosis and Systemic Endothelial Dysfunction: Retinal Correlations

Atherosclerosis occurs in large and small vessels including the retinal microcirculation, which are both characterized by endothelial dysfunction and chronic inflammation. The types of retinal vascular changes linked to atherosclerosis frequently occur before the apparent clinical cardiovascular outcomes, thus making them useful early predictors of disease in the system. It is worth mentioning that the constriction of retinal vessels and a decrease in the capillary perfusion are indicators of higher systemic vascular resistance and the worsening of endothelial function.[18] Although increased vascular permeability and leakage is conventionally assessed using fluorescein angiography, OCTA can also delicately determine the regions of increased blood flow and capillary dropout, which are early signs of atherosclerotic disease pathology.[18] Moreover, OCTA has been shown to identify retinal and choroidal hypoperfusion; research has shown that reduced choriocapillary blood flow is associated with atherosclerosis in the system and increased cardiovascular risk in the system.[18] The ability of OCTA to unveil the initial vascular deficits highlights its possible application in the cardiovascular risk assessment, especially since atherosclerosis plays a central role in the pathogenesis of ischemic heart disease and stroke.

4.4 Other CVD-Related Microvascular Abnormalities Detected via OCTA

In addition to atherosclerosis, diabetes, and hypertension, Optical Coherence Tomography Angiography (OCTA) is capable of identifying a range of retinal microvascular changes that are indicative of a broad range of cardiovascular diseases. Systemic circulatory insufficiency is common in patients with heart failure and it is seen through a decreased density of the retinal arteries and a broken choroidal perfusion, both of which can be visualised by OCTA.[19] Likewise, patients with increased vulnerability to ischemic stroke or those who have cerebrovascular disease might have such retinal microvascular defects as capillary dropout and worsening of the foveal avascular zone (FAZ), which act as early warning signs of cerebrovascular injury.[19] Also, within the framework of hyperlipidaemia and dyslipidaemia, OCTA is able to detect structural changes in retinal vessels and decreased capillary density, which may indicate endothelial dysfunction caused by lipid abnormalities and increased cardiovascular risk.[19] In accordance with these findings, Hannappe (2020) revealed that patients with coronary heart disease displayed markedly diminished retinal vessel density and an enlarged foveal avascular zone on OCTA relative to healthy controls, indicating that subclinical microvascular dysfunction in the retina corresponds with systemic atherosclerotic burden.[20]

CLINICAL IMPLICATIONS OF OCTA IN CARDIOVASCULAR RISK ASSESSMENT

OCTA is a useful technique for early diagnosis since it can identify microvascular changes before overt cardiovascular symptoms appear.⁶ The therapeutic importance of OCTA in cardiovascular risk assessment, its incorporation into screening procedures, and the difficulties in achieving broad use are all covered in this section.

5.1 OCTA's Potential as an Early CVD Diagnostic Tool

A decrease in retinal vessel density, expansion of the foveal avascular zone (FAZ), loss of choriocapillaris flow, microvascular tortuosity, and capillary dropout are retinal microcirculation features recorded by OCTA and have been associated with a higher risk of cardiovascular disease.[7] OCTA can offer a risk assessment and early treatment of cardiovascular events by offering a

quantitative, non-invasive assessment of microvascular health by measuring these biomarkers.

5.2 Integrating Retinal Imaging into Cardiovascular Screening Protocols

Introduction of retinal imaging in the cardiovascular risk evaluation is a progressive approach to preventive medicine. Since cardiovascular diseases do not manifest themselves in the majority of cases before the late stages, the possibility to introduce Optical Coherence Tomography Angiography (OCTA) into regular health assessment is a good chance to discover high-risk patients at earlier stages. OCTA may be integrated in routine screening tests of patients with known cardiovascular risk factors like those with hypertension, diabetes, and dyslipidaemia.[21] The application of OCTA to assess the retinal microvascular health in patients with diabetic retinopathy, a frequent comorbidity in endocrinology and diabetes clinics, may provide meaningful contributions to the management of cardiovascular disease by offering the information about the systemic dysfunction of the microvascular system used to monitor diabetic retinopathy.[21] In stroke prevention programme and neurology, OCTA has the potential to be used as a non-invasive stroke risk stratification tool, as retinal microvascular abnormalities have been linked to cerebrovascular events.[21] Similarly, in cardiology clinics, OCTA can be used as an adjunctive diagnostic tool to the traditional diagnostic tests like carotid ultrasound and coronary artery calcium score to provide a complementary source of information about systemic micro-vascular health.[21] Integration of OCTA into multidisciplinary clinical practices, thus, has the potential of enhancing early diagnosis, risk stratification, and personalised treatment of cardiovascular disease.

5.3 Challenges in Standardization and Clinical Adoption

The angiographic technique of optical coherence tomography (OCTA) has transformed the imaging of vascularity in the eye as a non-invasive technique to examine the retinal vascular structure.[22] Although it has a promising potential of cardiovascular screening, there are a number of challenges that need to be overcome in a bid to give it an opportunity to be incorporated in normal clinical practise. The main weakness is the lack of standardised diagnostic criteria; though OCTA shows potential in assessing microvascular health, at the present, there are no universally accepted cutoff values of cardiovascular risk factors like vessel density or FAZ size.[22] Moreover, inconsistency in imaging protocols and analysis is also a limitation, because the variability in OCTA equipment, image acquisition methods, and image-data analysis algorithms may cause variations in interpretation.[22] Angs et al. (2019) found a significant correlation between diminished retinal and choroidal vascular density on OCTA and heightened severity of coronary artery stenosis as assessed by Gensini scoring. Their findings strengthen the diagnostic capability of OCTA-derived vascular measures as non-invasive indicators of subclinical coronary microvascular impairment. [23]

The other important barrier is the lack of awareness of general practitioners and the cardiologists; since retinal imaging has always been limited to ophthalmology, its use in cardiovascular evaluation is not well-known among eye care specialists yet.[22] Additionally, there is a dire need of longitudinal research to define the prognostic utility of OCTA-based biomarkers to predict cardiovascular events. The available evidence is mostly cross-sectional, and the clinical utility of the evidence needs to be validated by strong prospective research.[22] Lastly, the barrier to access and affordability could limit the generalization of OCTA, especially in low-resource healthcare facilities, although its availability is increasing.[22]

To address such difficulties, the multi-disciplinary approach involving ophthalmologists, cardiologists, and public-health experts is necessary in order to develop standardised guidelines, confirm the relevance of systemic biomarkers produced by OCTA, and recommend its further use in cardiovascular practise. The retinal microvascular imaging that can be offered by OCTA is a valuable source of information on the state of the vascular system in general and has significant potential to develop into a non-invasive tool of early cardiovascular risk detection. Despite the fact that clinical application of OCTA is still in the developmental stage, current research and standardisation efforts might make it an essential part of multidisciplinary screening programmes. The inclusion of OCTA in prevention healthcare practices has the potential to improve patient outcomes, early diagnosis and reduce the burden of cardiovascular disease in the world as the correlation between retinal and systemic vascular health is becoming increasingly evident.

OCTA provides a quick, non-invasive method to visualise the health of retinal microvasculature, which corresponds to systemic vascular integrity. Integrating OCTA into cardiovascular screening may facilitate earlier diagnosis and enhanced surveillance of at-risk people.

FUTURE DIRECTIONS AND RESEARCH GAPS

In order to properly determine the importance of Optical Coherence Tomography Angiography (OCTA) in cardiovascular diagnostics, a number of research gaps and methodological issues need to be tackled although the potential of OCTA to assess the health of the systemic vascular is proven. The future research needs to consider standardisation of OCTA parameters to achieve wider clinical use, artificial intelligence (AI) to enhance image analysis and the validation of biomarkers obtained using OCTA.

6.1 Need for Large-Scale Longitudinal Studies on OCTA-Derived Biomarkers

The cross-sectional studies are effective in assessing risk factors related to a disorder.[24] They can be best used to describe disease-related characteristics or to establish how common a characteristic is in a particular cohort.[25] Currently, the evidence of the association between OCTA measurements on the one hand and cardiovascular disease (CVD) risk on the other hand is predominantly based on cross-sectional studies. Causality and prognostic value can only be determined through large-scale longitudinal studies. These studies should investigate the predictive power of retinal microvascular changes observed by OCTA in future cardiovascular events, including myocardial infarction and stroke, investigate how microvascular changes respond to

cardiovascular risk factors (e.g., diabetes, dyslipidaemia, hypertension), and establish standardised threshold values of OCTA measurements (e.g., vessel density, foveal avascular zone size) of the presence of high cardiovascular risk. Analytical cross-sectional studies can be used to preliminarily demonstrate causal relationships by aggregating prevalence data to determine the disparity in outcomes.[26] Long-term cohort studies and multicentre clinical trials will be essential to OCTA's validation as a cardiovascular health prediction tool.

6.2 AI and Machine Learning in Enhancing OCTA-Based Cardiovascular Assessments

The integration of artificial intelligence (AI) and machine learning (ML) into optical coherence tomography angiography (OCTA) analysis has the potential to enhance the diagnostic efficiency and accuracy of cardiovascular risk assessment. AI-powered methods can automate the detection of microvascular anomalies, thereby increase diagnostic consistency and reduce observer variability. Additionally, these technologies can analyze vast volumes of imaging data to detect subtle patterns associated with systemic vascular disorders. The incorporation of OCTA derived biomarkers with conventional cardiovascular risk factors such as blood pressure and cholesterol levels can further refine risk stratification models. Moreover, the combination of retinal imaging with other clinical data within machine learning algorithms holds promise for improving early disease detection. Maldonado-Garcia et al. (2025) demonstrated that deep-learning analysis of retinal OCT data can predict future cardiovascular events with higher accuracy than traditional clinical risk models, underscoring the prognostic potential of OCT-derived retinal biomarkers.[27] Overall, AI-assisted OCTA may substantially elevate the clinical utility of retinal imaging in cardiovascular diagnostics by enabling more accurate and scalable evaluations for routine screening. [24], [25]

6.3 Standardizing OCTA Metrics for Systemic Disease Monitoring

The major barrier to clinical use of OCTA in cardiovascular evaluations is the fact that imaging systems have not been standardised. This variability hinders the consistency and comparability of vessel density and flow measurements across devices and manufacturers. Future studies should, therefore, focus on the creation of universal OCTA imaging protocols that would provide measurement uniformity. Moreover, there is an urgent need to develop clinical reference values of biomarkers derived using OCTA in at-risk and healthy populations. It is also essential to develop standardised rules of data interpretation that can be used by general practitioners, cardiologists, and ophthalmologists equally, which will allow them to use it across disciplines. Finally, such standardisation initiatives will play a key role in establishing OCTA as a part of everyday clinical practise, as well as in establishing it as a stable tool in the monitoring of the state of systemic vascular health.

CONCLUSION

This review highlights significant findings that OCTA is very useful in identifying microvascular changes that are related to high blood pressure, diabetes mellitus, atherosclerosis, and other heart diseases. The retinal microvascular abnormalities can be a strong indicator of cardiovascular disease, as it provides a special insight into the condition of the whole systemic arteries. The inclusion of OCTA in cardiovascular screening practise may contribute to improved preventive measures and early diagnosis. However, some challenges are still present, especially the need to conduct longitudinal research and standardise OCTA measures. The interdisciplinary cooperation and AI-based analysis of images will become essential to establish OCTA a safe cardiovascular diagnostic procedure.

Abbreviation

FAZ- Foveal Avascular Zone
 CVD- Cardiovascular Disease
 OCTA- Optical Coherence Tomography Angiography
 SVP- Superficial Vascular Plexus
 DVP- Deep Vascular Plexus
 PD- Perfusion Density
 RPC- Radial Peripapillary Capillary
 VD- Vessel Density
 ICGA- Indocyanine Green Angiography

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REFERENCES:

1. W. H. O. WHO, "Cardiovascular diseases (CVDs)." 2025. [Online]. Available: [https://www.who.int/news-room/fact-sheets/detail/cardiovascular-diseases-\(cvds\)](https://www.who.int/news-room/fact-sheets/detail/cardiovascular-diseases-(cvds))
2. M. Di Cesare *et al.*, "The heart of the world," *Glob. Heart*, vol. 19, no. 1, p. 11, 2024.
3. R. S. Vasan, "Biomarkers of cardiovascular disease: molecular basis and practical considerations," *Circulation*, vol. 113, no. 19, pp. 2335–2362, 2006.
4. T. Chaikijurajai, J. P. Ehlers, and W. H. W. Tang, "Retinal microvasculature: a potential window into heart failure prevention," *Heart Fail.*, vol. 10, no. 11, pp. 785–791, 2022.
5. H. Hanssen, L. Streese, and W. Vilser, "Retinal vessel diameters and function in cardiovascular risk and disease," *Prog. Retin. Eye Res.*, vol. 91, p. 101095, 2022.

6. H. Liu and H. Wang, "Early detection system of vascular disease and its application prospect," *Biomed Res. Int.*, vol. 2016, no. 1, p. 1723485, 2016.
7. P. H. Le, K. Kaur, and B. C. Patel, "Optical coherence tomography angiography." 2024. [Online]. Available: <https://www.ncbi.nlm.nih.gov/books/NBK563235/>
8. R. F. Spaide, J. G. Fujimoto, N. K. Waheed, S. R. Sadda, and G. Staurenghi, "Optical coherence tomography angiography," *Prog. Retin. Eye Res.*, vol. 64, pp. 1–55, 2018.
9. Y. Sun and L. E. H. Smith, "[WITHDRAWN] retinal vasculature in development and diseases," *Annu. Rev. Vis. Sci.*, vol. 4, no. 1, pp. 101–122, 2018.
10. J. W. Kiel, "Anatomy." 2010. [Online]. Available: <https://www.ncbi.nlm.nih.gov/books/NBK53329/>
11. A. Das and J. Byrd, "Retinal vasculature: structure and pathologies," 2014.
12. "Optical coherence tomography angiography changes in cardiovascular systemic diseases and risk factors : A Review," pp. 1–15, 2022, doi: 10.1111/aos.14851.
13. A. H. Kashani *et al.*, "Optical coherence tomography angiography: a comprehensive review of current methods and clinical applications," *Prog. Retin. Eye Res.*, vol. 60, pp. 66–100, 2017.
14. T. E. De Carlo, A. Romano, N. K. Waheed, and J. S. Duker, "A review of optical coherence tomography angiography (OCTA)," *Int. J. Retin. Vitr.*, vol. 1, no. 1, p. 5, 2015.
15. J. I. E. Wang, S. Yuan, J. Qi, Q. Zhang, and Z. Ji, "Advantages and prospects of optical coherence tomography in interventional therapy of coronary heart disease (Review)," pp. 1–19, 2022, doi: 10.3892/etm.2022.11180.
16. M. Zakir *et al.*, "Cardiovascular complications of diabetes: from microvascular to macrovascular pathways," *Cureus*, vol. 15, no. 9, 2023.
17. R. Pahwa and I. Jialal, "Atherosclerosis." 2023. [Online]. Available: <https://www.ncbi.nlm.nih.gov/books/NBK507799/>
18. J. Chua *et al.*, "Optical coherence tomography angiography of the retina and choroid in systemic diseases," *Prog. Retin. Eye Res.*, vol. 103, p. 101292, 2024.
19. D. K. Prasad *et al.*, "A multi-stage approach for cardiovascular risk assessment from retinal images using an amalgamation of deep learning and computer vision techniques," *Diagnostics*, vol. 14, no. 9, p. 928, 2024.
20. M. A. Hannappe *et al.*, "Vascular density with optical coherence tomography angiography and systemic biomarkers in low and high cardiovascular risk patients," *Sci. Rep.*, pp. 1–9, 2020, doi: 10.1038/s41598-020-73861-z.
21. O. I. Runsewe, S. K. Srivastava, S. Sharma, P. Chaudhury, and W. H. W. Tang, "Optical coherence tomography angiography in cardiovascular disease," *Prog. Cardiovasc. Dis.*, vol. 87, pp. 60–72, 2024.
22. E. E. Pérez-Guerrero *et al.*, "Methodological and statistical considerations for cross-sectional, case–control, and cohort studies," *J. Clin. Med.*, vol. 13, no. 14, p. 4005, 2024.
23. J. W. Ang, J. J. Iang, Y. Z. Hang, Y. W. Q. Ian, and J. F. Z. Hang, "Retinal and choroidal vascular changes in coronary heart disease : an optical coherence tomography angiography study," vol. 10, no. 4, pp. 1532–1544, 2019, doi: 10.1364/BOE.10.001532.
24. D. Antay-Bedregal, E. Camargo-Revello, and G. F. Alvarado, "Associated factors vs risk factors in cross-sectional studies," *Patient Prefer. Adherence*, pp. 1635–1636, 2015.
25. B. Capili, "Cross-sectional studies," *AJN Am. J. Nurs.*, vol. 121, no. 10, pp. 59–62, 2021.
26. D. T. Reddy *et al.*, "The role of artificial intelligence in healthcare: enhancing coronary computed tomography angiography for coronary artery disease management," *Cureus*, vol. 16, no. 6, 2024.
27. C. Maldonado-garcia *et al.*, "Predicting risk of cardiovascular disease using retinal optical coherence tomography imaging," no. Mi.
28. M. G. Cerdas *et al.*, "The role of artificial intelligence and machine learning in cardiovascular imaging and diagnosis: current insights and future directions," *Cureus*, vol. 16, no. 10, 2024.
29. I. Yasser, F. Khalifa, H. Abdeltawab, M. Ghazal, H. S. Sandhu, and A. El-Baz, "Automated diagnosis of optical coherence tomography angiography (OCTA) based on machine learning techniques," *Sensors*, vol. 22, no. 6, p. 2342, 2022.