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Assessing the retinal microvasculature in heart failure: a systematic review and possible clinical implications

Vanreusel, I; Van Eijgen, J; Jena, F; Vermeulen, D; Gevaert, A; Van Craenenbroeck, A; Cornelissen, V; Van Aelst, LN; Van Edom, C; Van Berendoncks, A; Segers, V; Stalmans, I; Van Craenenbroeck, E.

Corresponding author:
Inne Vanreusel

inne.vanreusel@uantwerpen.be

Author Affiliation:
Antwerp University Hospital.

ADMINISTRATIVE INFORMATION

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Review Stage at time of this submission - Data analysis.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 24 May 2024 and was last updated on 30 September 2025.

INTRODUCTION

Review question / Objective To summarize the current literature on retinal vascular imaging parameters in HF, with particular focus on pathophysiology, therapeutic implications, and their potential use as markers of HF risk, severity and prognosis.

Rationale Despite significant progress in pharmacological and device therapy of heart failure (HF), its long-term prognosis remains poor, and its pathophysiology is incompletely understood. Microvascular function is impaired early in the development and progression of many pathological processes like HF. Retinal imaging provides a unique opportunity for easy, non-invasive and early detection of systemic microvascular disease.

Condition being studied Heart failure is a chronic condition where the heart is unable to pump blood efficiently to meet the body's needs. This can result from various underlying conditions that damage or overwork the heart muscle, such as cardiovascular comorbidities (like high blood pressure or obesity), coronary artery disease, cardiomyopathies, arrhythmias, heart valve disease…

Key characteristics of heart failure include:
* Symptoms: Common symptoms include shortness of breath, fatigue, swollen legs, and rapid heartbeat.
* Types: Heart failure is often classified into two main types: heart failure with reduced ejection fraction (HFrEF) and heart failure with preserved ejection fraction (HFpEF)

Heart failure is a serious condition that requires ongoing management and can significantly impact quality of life .

METHODS

Search strategy A literature search using MEDLINE (Pubmed), EMBASE (Ovid), Web of Science (Clarivate Analytics) and Cochrane Library (Cochrane), based on two concepts:
* First concept: "Retinal vasculature"
* Second concept: "Non-ophthalmic disease," including heart failure, chronic kidney disease, glaucoma, and cerebral small vessel disease.
with search terms for each concept adjusted according to the database (details available in Supplementary Material 1).

Note: Initially, studies on retinal vasculature were sought in a broad population, specifically patients with heart failure, chronic kidney disease, glaucoma, and cerebral small vessel disease. Due to the extensiveness of the information obtained, it was decided to split the results into separate review articles. For this review, we focused on patients with heart failure.

Participant or population Patients with heart failure.

Intervention Assessment of the retinal vasculature by different techniques.

Comparator NA.

Study designs to be included Both analytic studies (experimental and observational) studies and (systematic) reviews/meta-analyses.

Eligibility criteria
Exclusion criteria:
i. Studies performed in children and adolescents
ii. Studies solely on retrobulbar vessels
iii. Molecular or genetic research
iv. Editorials, conference abstracts or case reports
v. No full-text available online through the institutional access of the University of Antwerp or KU Leuven, or via ResearchGate
vi. Studies in languages other than English
vii. Animal research.

Information sources Electronic databases: MEDLINE (Pubmed), EMBASE (Ovid), Web of Science (Clarivate Analytics) and Cochrane Library (Cochrane). In addition: search through the reference lists of the included articles to identify further relevant articles.

Main outcome(s)
* Presence of abnormalities in the retinal vasculature in HF
* Clinical relevance of abnormalities in the retinal vasculature in HF
– Do retinal vascular alterations predict the risk of developing HF and predict HF prognosis?
– Do retinal vascular alterations correlate with HF severity?
– Do alterations in the retinal vasculature reflect alterations in other vascular beds?

Additional outcome(s)
Give an overview of:
– Retinal microvascular anatomy, physiology and imaging techniques
– Pathophysiology underlying retinal vasculature abnormalities in HF
– Retinal vasculature as outcome measure in therapeutic or interventional studies for HF.

Data management Two reviewers independently entered relevant data into a pre-designed data extraction table. The extracted data were cross-checked and the reviewers resolved any discrepancies through discussion until a consensus was achieved.

Quality assessment / Risk of bias analysis The included studies were evaluated for quality using the Quality Assessment Tools from the National Heart, Lung, and Blood Institute by two independent investigators.

Strategy of data synthesis A PRISMA flow diagram was constructed for the number of articles excluded and included. The full texts of the included articles were thoroughly reviewed by two reviewers. These two reviewers independently entered relevant data into a pre-designed data extraction table, including the first author's name and country, publication year, study design, and main outcomes (for all studies), search strategy (for reviews), and retinovascular assessment method, number of subjects, and characteristics of the study groups (for primary studies). Based on this information, all research questions were answered, and where necessary, tables and figures were constructed to provide more detailed information.

Subgroup analysis None.

Sensitivity analysis NA.

Language restriction English.

Country(ies) involved Belgium.

Keywords heart failure, retinal microvasculature, microvascular function, microvascular dysfunction.

Dissemination plans We aim to publish this systematic review in a prestigious Heart Failure journal with high impact.

Contributions of each author

Author 1 - Inne Vanreusel - performed the quality assessment of the articles, data extraction and drafted and completed the writing of the manuscript.
Author 2 - Jan Van Eijgen - performed the literature search, screening of articles, quality assessment of the articles, data extraction and completed the writing of the manuscript.
Author 3 - Freya Jena - performed the literature search, screening of articles and drafted the writing of the manuscript.
Author 4 - Dorien Vermeulen - read, provided feedback and approved the final manuscript.
Author 5 - Andreas B. Gevaert - read, provided feedback and approved the final manuscript.
Author 6 - Amaryllis H. Van Craenenbroeck - read, provided feedback and approved the final manuscript.
Author 7 - Véronique Cornelissen - read, provided feedback and approved the final manuscript.
Author 8 - Lucas N. L. Van Aelst - read, provided feedback and approved the final manuscript.
Author 9 - Charlotte Van Edom - read, provided feedback and approved the final manuscript.
Author 10 - An Van Berendoncks - read, provided feedback and approved the final manuscript.
Author 11 - Vincent F.M. Segers - read, provided feedback and approved the final manuscript.
Author 12 - Ingeborg Stalmans - contributed to the article concept and the development of the selection criteria, guided the writing of the article and approved the final manuscript.
Author 13 - Emeline M. Van Craenenbroeck - contributed to the article concept and the development of the selection criteria, guided the writing of the article and approved the final manuscript.