

# INPLASY

## Assessing the retinal microvasculature in heart failure: a systematic review and clinical guidance

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### ADMINISTRATIVE INFORMATION

**Support** - Fund for Scientific Research Flanders.

**Review Stage at time of this submission** - Data analysis.

**Conflicts of interest** - None declared.

**INPLASY registration number:** INPLASY202450114

**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 24 May 2024.

## 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
- ii. Studies solely on retrobulbar vessels
- iii. Molecular or genetic research
- iv. Editorials, conference abstracts or case reports
- v. No full-text available
- vi. Studies in other languages 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)** \* Prevalence of abnormalities in the retinal vasculature in HF

\* Clinical relevance of abnormalities in the retinal vasculature in HF

– Do retinal vascular alterations influence the risk of developing HF and 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:

– Anatomy and physiology of blood flow regulation in the retinal microvasculature

– Pathophysiology behind abnormalities in the retinal vasculature in HF

– Therapies or interventions targeting retinal vasculature alterations in 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.

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**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 - Andreas Gevaert - read, provided feedback and approved the final manuscript.

Author 5 - Amaryllis Van Craenenbroeck - read, provided feedback and approved the final manuscript.

Author 6 - Veronique Cornelissen - read, provided feedback and approved the final manuscript.

Author 7 - An Van Berendoncks - read, provided feedback and approved the final manuscript.

Author 8 - Vincent Segers - read, provided feedback and approved the final manuscript.

Author 9 - 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 10 - Emeline 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.