INPLASY

INPLASY2024100121

doi: 10.37766/inplasy2024.10.0121

Received: 28 October 2024

Published: 28 October 2024

Corresponding author:
Inne Vanreusel

inne.vanreusel@uantwerpen.be

Author Affiliation:
Antwerp University Hospital.

Assessment of the retinal microvasculature in congenital heart disease: a systematic review

Vanreusel, I; Van Eijgen, J; Moons, P; Van De Bruaene, A; Budts, W; Bruyndonckx, L; Stalmans, I; Van Berendoncks, A.

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: INPLASY2024100121

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 28 October 2024 and was last updated on 30 December 2025.

INTRODUCTION

Review question / Objective To summarize the literature published over the last decade regarding retinovascular imaging parameters in non-syndromic children, adolescents and adults with congenital heart disease with particular focus on pathophysiology, therapeutic implications, the potential of surrogate markers for disease severity, and prognosis.

Rationale Despite advancements in surgical techniques and clinical treatments, congenital heart disease (CHD) remains associated with high morbidity and mortality rates. Improving therapy and preventive strategies necessitates a deeper understanding of the underlying pathophysiological mechanisms in CHD.
Microvascular dysfunction emerges early in the development and progression of numerous pathological conditions. These changes in the microvasculature represent among the earliest signs of target organ damage and are predictive for cardiovascular mortality and prognosis. Therefore, evaluation of the microcirculation holds promise for cardiovascular risk stratification. While assessment of the microcirculation can be conducted in various vascular beds, the retina stands out as a unique window for in vivo assessment of the microvasculature and its disorders in a non-invasive manner. Recently, there has been a growing interest in the evaluation of the retinal microcirculation, including within the context of CHD.

Condition being studied * Congenital heart disease (CHD) refers to a structural abnormality of the heart present at birth, resulting from improper development of the heart or blood vessels during fetal growth. These defects can affect the heart's walls, valves, or major arteries and veins, leading to impaired circulation of blood throughout the body.
CHD is one of the most frequently diagnosed congenital disorders, affecting approximately 1% of live births worldwide. Patients with CHD are a heterogeneous population in terms of both anatomical and physiological characteristics, as

well as in the nature of surgical repair or palliation. Even after successful treatment (in childhood), CHD patients are not fully cured of their condition. The majority of adults with CHD will eventually experience complications related either to their original heart defect or to the surgical procedures performed, although these complications may not become apparent for many years. As a result, managing the lifelong care of these patients has become increasingly critical.
* Microvascular dysfunction (MVD) refers to the abnormal function of small blood vessels (microvasculature), particularly in their ability to regulate blood flow and oxygen delivery to tissues. It occurs when these vessels fail to dilate or constrict properly in response to physiological needs. MVD may result from various pathophysiological mechanisms, including structural and functional aberrations of the microvasculature, along with extravascular changes and is often due to endothelial dysfunction, inflammation, or oxidative stress. Microvascular dysfunction plays a key role in cardiovascular disease.

METHODS

Search strategy A literature search was performed using MEDLINE (Pubmed), EMBASE (Ovid), Web of Science (Clarivate Analytics) and Cochrane Library (Cochrane), based on two concepts (details available in Supplementary Materials):
* 1st concept: “Retinal vasculature”
* 2nd concept: “Congenital Heart Disease”
Studies on retinal vasculature in patients with CHD published from January 1, 2014 until December 31, 2023 were included.

Participant or population Patients (children, adolescents and adults) with congenital heart disease.

Intervention Assessment of the retinal vasculature by different techniques.

Comparator NA.

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

Eligibility criteria
Exclusion criteria:
* Studies solely evaluating retinopathy of prematurity
* Studies performed in syndromic patients
* Molecular or genetic research
* No full-text available
* Editorials, conference abstracts or case reports
* Studies in other languages than English
* 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 CHD
* Pathophysiology behind abnormalities in the retinal vasculature in CHD
* Clinical relevance of abnormalities in the retinal vasculature in CHD
- Retinal vascular alterations and their relationship to other vascular beds
- Retinal vascular alterations and CHD severity
- Retinal vascular alterations and CHD prognosis
* Therapeutic interventions targeting retinal vasculature alterations in CHD.

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 first author’s name and country, publication year and study design. For primary studies, the assessment method with the retinovascular parameters and reported results were collected alongside the descriptives of the study group(s). For CHD (further subdivided into subgroups if relevant), these descriptives include types of CHD, age group, surgical history, and number of subjects. For the healthy control groups (if provided), these include the parameters used for matching with CHD, differences in cardiovascular risk factors compared to CHD, and number of subjects. For reviews, the collected information encompasses the research question (including the

type(s) of CHD and age group), the search strategy, and the main outcomes. Based on this information, all research questions were answered, and where necessary, tables and figures were constructed to provide more detailed information.

Subgroup analysis Studies examining the ocular microvasculature in CHD are traditionally divided into 3 categories: patients with coarctation of the aorta, those with cyanotic CHD, and heterogeneous groups encompassing a broad spectrum of CHD types. We have adopted a similar classification.

Sensitivity analysis NA.

Language restriction English.

Country(ies) involved Belgium.

Keywords retinal microvasculature, microvascular function, microvascular dysfunction, congenital heart disease, congenital heart defect.

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

Contributions of each author

Author 1 - Inne Vanreusel - performed the literature search, screening of articles, quality assessment of the articles, data extraction 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 - Philip Moons - read, provided feedback and approved the final manuscript.
Author 4 - Alexander Van De Bruaene - read, provided feedback and approved the final manuscript.
Author 5 - Werner Budts - read, provided feedback and approved the final manuscript.
Author 6 - Luc Bruyndonckx - read, provided feedback and approved the final manuscript.
Author 7 - 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 8 - An Van Berendoncks - contributed to the article concept and the development of the selection criteria, guided the writing of the article and approved the final manuscript.