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Original Article

# Retinal fluorescein angiography: A sensitive and specific tool to predict coronary slow flow

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ABSTRACT

*Background:* Obstructive coronary artery disease (OCAD) and coronary slow flow (CSF) are frequent angiographic findings for patients that have chest pain and require frequent hospital admission. The retina provides a window for detecting changes in microvasculature relating to the development of cardiovascular diseases such as arterial hypertension or coronary heart disease.
*Objectives:* To assess the coronary and ocular circulations in patients with CSF and those with obstructive coronary artery disease.
*Methods:* A prospective study was conducted over 3.5 years, included a total of 105 subjects classified to 4 groups: *Group I (OCAD)*: Included 30 patients with obstructive coronary artery disease, *group II (CSF)*: Included 30 patients with coronary slow-flow, *group III (Control 1)*: Included 30 healthy control persons and *group IV (Control 2)*: Included 15 patients indicated for coronary angiography that proved normal. All participants were subjected to coronary angiography (except control group 1), ophthalmic artery Doppler for measuring Pulsatility index (PI) and resistivity index (RI) and Fluorescence angiography of retinal vessels.
*Results:* Patients with CSF showed slow flow retinal circulation (microcirculation) evidenced by prolonged fluorescein angiography (Arm-retina time [ART] & Arterio-venous Transit time [AVTT]). Ophthalmic artery Doppler measurements (RI & PI) were significantly delayed in OCAD and CSF patients. There was significant positive correlation between TIMI frame count in all subjects and ART, AVTT, PI, RI and Body Mass Index. Using ART cutoff value of >16 s predicted CSF with sensitivity and specificity of 100%, meanwhile AVTT of >2 s predicted CSF with a sensitivity 96.7% and specificity of 93.3.
*Conclusion:* Both delayed arm-retina time and retinal arterio-venous transit times can accurately predict coronary slow-flow.


## 1. Introduction

Coronary slow-flow (CSF) is an angiographic finding observed in patients with normal or near-normal coronary arteries. It is characterized by delayed opacification of coronary arteries during angiography and was initially reported in 1972 by Tambe et al.[1] The frequency of CSF is approximately 1–5% in patients undergoing coronary angiography. More than 80% of patients with CSF often experience recurrent chest pain; almost 20% require readmission following the same diagnosis.[2] Also, CSF has been linked to parameters of poor prognosis, including fatal arrhythmias and sudden cardiac death.[2] It is still not clear whether or not the coronary slow flow is a focal or a systemic disturbance of the vasculature that may occur simultaneously in other territories of the circulation.[3]

Over the last 8–10 years, multiple large prospective cohort studies examining the relationship between retinal vascular changes and clinical endpoints of coronary disease, and there was strong positive correlation between the two, also an association between retinal microvascular abnormalities and markers of subclinical or microvascular coronary disease has been detected.[4] The retina is a unique site where the microcirculation can be imaged directly. Thus, it provides a window for detecting changes in microvasculature relating to the development of cardiovascular

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diseases such as arterial hypertension or coronary heart disease.[5] Retinal vascular imaging is explored in clinical settings as a risk stratification tool to aid clinicians in identifying patients with microvascular signs who are at high risk of future clinical cardiovascular and cerebrovascular events.[6]

The aim of this study is to assess if there is correlation between coronary and ocular circulations in patients with CSF and those with obstructive coronary artery disease in comparison to control persons.

## 2. Patients and methods

This is a prospective study which was carried out in the departments of cardiology and ophthalmology Minia University, Egypt during the period from October 2011 to May 2015. 105 subjects in this study were evaluated and classified into four groups as follow:

**Group I (OCAD)**: Included 30 patients with obstructive coronary artery disease.
**Group II (CSF)**: Included 30 patients with coronary slow-flow.
**Group III (Control 1)**: Included 30 healthy control persons.
**Group IV (Control 2)**: Included 15 patients with normal coronary angiogram.

Patients of group I were included with criteria of typical anginal pain, findings compatible with myocardial ischemia on diagnostic procedures and significant obstructive coronary arteries on angiography with 50% stenosis or more. Patients of group II were included with criteria of typical anginal pain, findings compatible with myocardial ischemia on diagnostic procedures and coronary slow flow on coronary angiography and diagnosed by TIMI Frame Count (TFC). As per group III (control 1), participants were chosen by being age and sex matching group I and II while having no history of chest pain and no findings compatible with myocardial ischemia on diagnostic procedure. Group IV (control 2) patients had chest pain, positive or equivocal diagnosis of ischemia on noninvasive procedure and normal coronary angiography.

Persons with history of previous myocardial infarction, coronary intervention or coronary artery bypass graft (CABG), moderate or severe valvular heart disease, hypertrophic, dilated and restrictive cardiomyopathy, diabetes; hypertension, obesity (BMI $\geq 30\ kg/m^2$) and other coronary artery diseases as myocardial bridging were excluded from the study.

All subjects included in this study were subjected to the following

1. Coronary Angiography study: All subjects in the study except group III underwent coronary angiography after informed consent with mention of possible complications. TFC was calculated using the method of Gibson et al.[7]
2. Ophthalmic artery Doppler study: For all subjects, the right or left eye was evaluated by color Doppler imaging with gel applied to closed eye lids, insuring no pressure applied on the globe with the probe during measurement. Doppler study was carried out with 7.5 MHz linear transducer and sample volume set at 1 mm and placed in the color Doppler images of the artery then peak systolic velocity (PSV), end diastolic velocity (EDV), pulsatility index (PI) and resistance index (RI) were automatically calculated by the machine (Fig. 1).
3. Fluorescence angiography of retinal vessels: All subjects underwent fluorescence angiography of retinal circulation after exclusion of contraindications with adequate pupillary dilatation while the patient is seated in front of fundus camera. Red free images were captured after 5 ml of a 10% sodium fluorescein is administrated intravenously into an antecubital vein over 2–3 s. The images were taken at approximately one second intervals over 25 s after injection according to Prall et al.[8] We calculated two time intervals: 1- Arterial phase (arm- to retinal time ART): time from injection until the dye first appears in the central retinal artery. It can vary between 7 to 15 s and represents systemic venous and arterial circulation flow. 2-Retinal arteriovenous transit time AVTT: time from the first appearance of dye in the temporal retinal arteries of the arcades to the time when the corresponding veins are completely filled. It is considered to be 1–2 s after the arterial phase.

Statistical analysis was done using SPSS 20 software package. Categorical data were presented as frequencies and percentages. Quantitative data were expressed as mean and standard deviation. Kolmogorov-Smirnov for normality test was used to differentiate between parametric data and non-parametric data. One way ANOVA test was used to test the significance between groups for quantitative variables meanwhile, Chi-square ($x^2$) was used for qualitative data. Duncan multi-comparison test was also used. Person correlation coefficient was used to get the correlation between variables. Sensitivity, specificity and accuracy were calculated. Probability (p. value) was considered significant if was <0.05.

## 3. Results

The results showed that there was no statistically significant difference regarding age, gender, diastolic blood pressure (DBP),

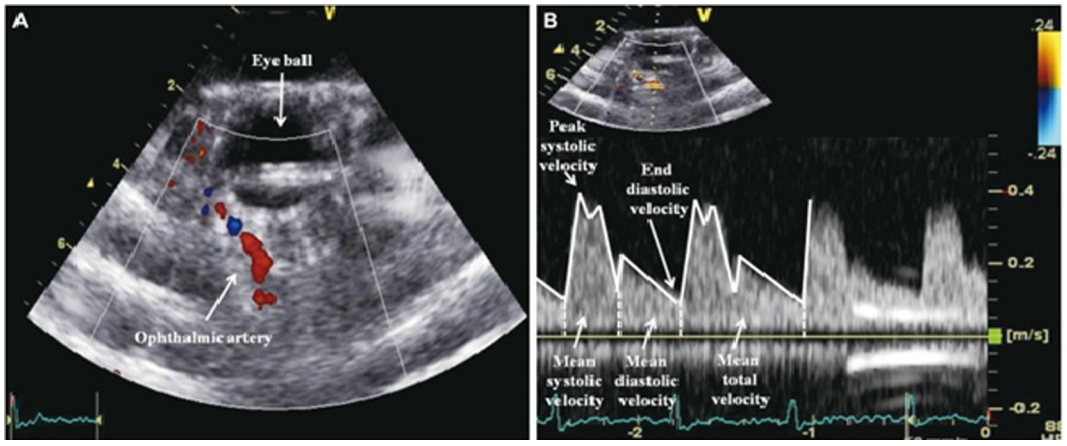


**Fig. 1.** Colour Doppler imaging measures velocity in ophthalmic artery.

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