

## Abnormality in coronary slow flow phenomenon detected by nailfold microcirculation microanalysis

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*To the Editor:* The coronary slow flow phenomenon (CSFP) was first reported by Tambe *et al* in 1972.<sup>[1]</sup> Specifically, patients suffering from chest pain but without significant coronary artery lesion, displayed slow coronary blood flow during coronary angiography examination, which could lead to myocardial ischemia, acute myocardial infarction, and acute coronary syndrome. The development of CSFP has been reported to be around 7% in patients with suspected coronary heart disease.<sup>[2]</sup> The common clinical symptoms during CSFP include slow opacification of distal parts of normal epicardial coronary arteries in the absence of ventricular dysfunction, connective tissue disorder, valvular heart diseases, and coronary spasm or ectasia. Nowadays, the identification of the CSFP is achieved through coronary angiography by thrombolysis in myocardial infarction (TIMI) flow grade. The corrected TIMI frame count (CTFC) is a very common, simple, and repeatable method used for the quantification of the coronary flow.<sup>[3]</sup>

However, non-invasive methods to detect CSFP are still scarce. Nailfold capillaroscopy could be used as an alternative, simple and non-invasive method to study the microvasculature of CSFP by magnifying and evaluating the morphology of nailfold capillaries.<sup>[4]</sup> Changes of nailfold capillaries have been observed to identify various rheumatic disorders, especially systemic sclerosis.<sup>[4]</sup> Additional studies reported that nailfold capillaroscopy was a useful technique for microvascular analysis in cases of dermatomyositis, systemic lupus erythematosus, Sjögren syndrome, antiphospholipid syndrome, and familial Mediterranean fever. In 2014, Serkan *et al*<sup>[5]</sup> observed nailfold capillary abnormalities, such as dilatation, tortuosity, and microhemorrhage, in the microvasculature of CSFP patients by video dermatoscopy, with dilatation as the most common detected abnormality. However, the evaluation of nailfold capillaroscopy in coronary flow of CSFP patients remains unexplored.

In this study, with nailfold microcirculation microanalyzer, we compared the nailfold capillaries, coronary angiography, and clinical parameters between patients with CSFP and normal healthy controls. The demographic characteristics and laboratory parameters of CSFP and normal coronary flow (NCF) groups were presented in Supplementary Table 1 [Supplementary Table 1, <http://links.lww.com/CM9/A496>]. All the parameters between CSFP and the NCF group have no significant difference except for the active nicotine use (smokers), which was higher in the CSFP group ( $P < 0.05$ ).

The TIMI frame count showed a different distribution pattern of CSFP between CSFP group and NCF group: 38 (76%) patients had CSFP in left anterior descending (LAD); eight (16%) patients had CSFP in right coronary artery (RCA); four (8%) patients had CSFP in left circumflex artery (LCX); 20 (40%) patients had CSFP in LAD and RCA; three (6%) patients had CSFP in LAD and LCX; one (2%) patient had CSFP in RCA and LCX and 11 (22%) patients had CSFP in LAD, LCX, and RCA [Supplementary Table 2, <http://links.lww.com/CM9/A497>]. Notably, the CTFC values for all epicardial coronary arteries and mean CTFC were significantly higher in CSFP group than that in the NCF group ( $P < 0.001$ ) [Supplementary Table 2, <http://links.lww.com/CM9/A497>].

Nailfold capillary morphology of the CSFP and NCF groups were shown in Supplementary Table 3, <http://links.lww.com/CM9/A498>. Capillary morphology abnormalities were detected in nine (18%) patients in NCF group and 12 (24%) in CSFP group [Figure 1]. There was no significant difference in morphology between the two groups ( $P = 0.461$ ). In NCF group, the capillary loops of the nailfold microcirculation were hairpin-shaped, straight, parallel to the input and output branches, with a diameter ratio of 1:1.5. The blood vessels were clear, well arranged and evenly distributed [Figure 1A]. The capillary morphology of the CSFP group had nearly the same morphology, but the diameter of input branch, output

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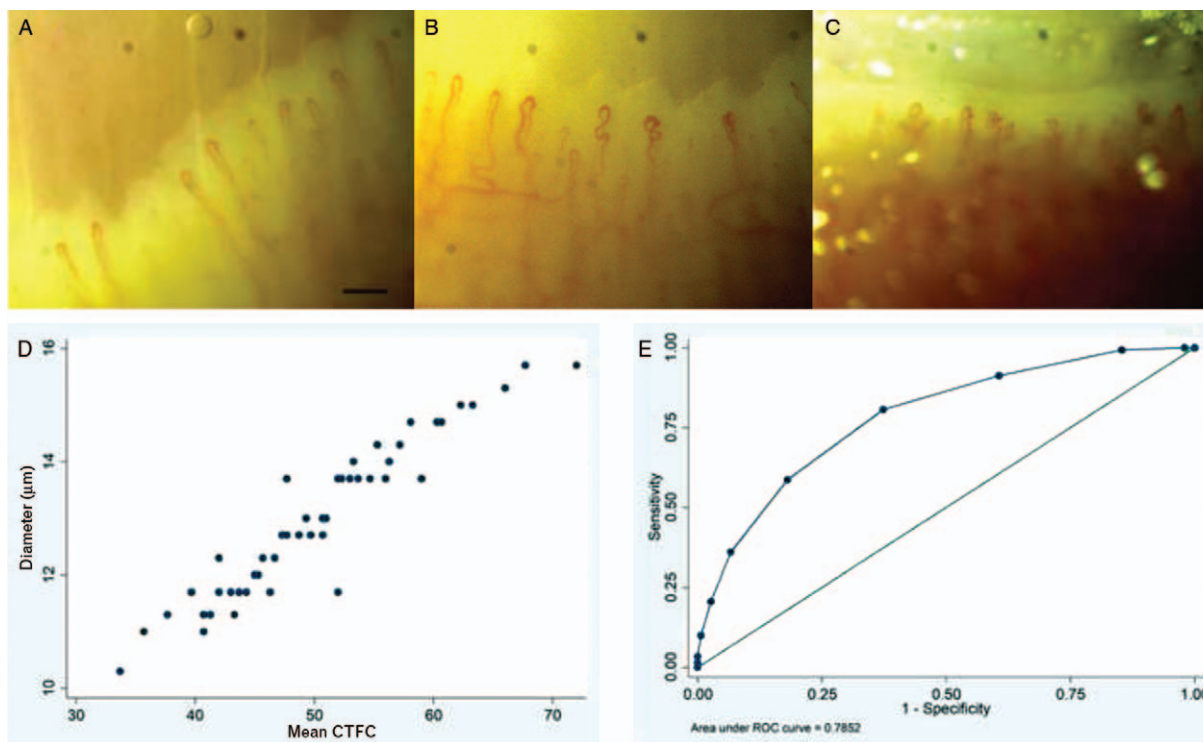
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**Figure 1:** The nailfold capillary morphology of the CSFP ( $n = 50$ ) and NCF group ( $n = 50$ ). (A) Normal (NCF group); (B) Dilatation (CSFP group); (C) Tortuosity; The size bar indicated  $10 \mu\text{m}$ ; (D) The association of nailfold capillary diameter and mean CTFC in the CSFP group. (E) The ROC curve of nail fold capillary diameter. CSFP: Coronary slow flow phenomenon; CTFC: Corrected TIMI frame count; NCF: Normal coronary flow; ROC: Receiver operating characteristic.

branch, and loop top in CSFP patients were thicker than that of normal control ones [Figure 1B]. In Figure 1C, the capillary loops were arranged disorderly and folded repeatedly, which was defined as tortuosity. There was no capillary morphology abnormality of microhemorrhage in both CSFP and NCF groups. Supplementary Table 4, <http://links.lww.com/CM9/A499> showed the nailfold capillary diameter of CSFP and NCF group. The results indicated that the diameters of capillary input branch, output branch, loop top, and mean diameter were larger in CSFP group compared with that in control ones ( $P < 0.05$ ).

The results showed that there was a strong positive correlation between mean CTFC and capillary diameter in the CSFP group ( $r = 0.9518$ ,  $P < 0.001$ ) [Figure 1D], which indicated that the diameter of capillary was increased as the blood flow velocity of coronary was slowed down. Receiver operating characteristic curve analysis showed that nail fold capillary diameter occupied more than 0.7 of the area under curve (AUC) ( $\text{AUC} = 0.7852$ ) [Figure 1E], indicating that nail fold capillary diameter can be used to evaluate CSFP.

CSFP is more common in males, smokers, patients with dyslipidemia, metabolic syndrome, and Obesity. In our study, we confirmed CSFP occurred more commonly among smokers. Furthermore, asymptomatic smokers, with no evidence of coronary artery disease, have shown coronary microvascular dysfunction with 21% reduction of the coronary flow reserve compared to the value of the non-smoking control population.

In addition, we found that the diameter of nailfold capillary was enlarged in CSFP patients. This result was not only consistent with the finding by Serkan *et al*<sup>[5]</sup> who found nailfold capillary was dilated by nailfold capillaroscopy, but also could be considered as a further quantitative study. Linear correlation regression analysis showed that CTFC increased with the nailfold capillary diameter in CSFP group. The mechanism may be that capillary compensatory dilatation is needed to maintain tissue blood supply and oxygen demand when microcirculatory blood flow slows down. The AUC area ( $\text{AUC} = 0.7852$ ) was calculated from the operation curve of the subjects, which indicated that the diameter of nailfold capillary could be used to evaluate CTFC.

In conclusion, our study provided a non-invasive method, suggesting that the nailfold microcirculation microanalyzer could be used to diagnose and monitor the CSFP on a routine basis. Furthermore, this method is very convenient, which has a low cost and repeatable result. The medical therapeutic processes used for the treatment of CSFP could be also verified by nailfold capillaroscopy. Therefore, our study indicated that nailfold microcirculation microanalysis is a simple, promising, and reproducible technology that can be used to detect abnormalities in CSFP instead of the classic coronary angiography.

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### Conflicts of interest

None.

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