Prevalence and predictors of slow coronary flow phenomenon in Kermanshah province

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Abstract

Introduction: This study was conducted to investigate prevalence and predictors of slow coronary flow phenomenon (SCF) phenomenon.

Methods: This cross-sectional study was performed at Imam Ali Cardiovascular Hospital affiliated with the Kermanshah University of Medical Sciences (KUMS), Kermanshah province, Iran. From March 2017 to March 2019, all the patients who underwent coronary angiography were enrolled in this study. Data were obtained using a checklist developed based on the study's aims. Independent samples t tests and chi-square test (or Fisher exact test) were used to assess the differences between subgroups. Multiple logistic regression model was applied to evaluate independent predictors of SCF phenomenon.

Results: In this study, 172 (1.43%) patients with SCF phenomenon were identified. Patients with SCF were more likely to be obese (27.58 ± 3.28 vs. 24.12 ± 3.26, P < 0.001), hyperlipidemic (44.2 vs. 31.7, P < 0.001), hypertensive (53.5 vs. 39.1, P < 0.001), and smoker (37.2 vs. 27.2, P = 0.006). Mean ejection fraction (EF) (51.91 ± 6.33 vs. 55.15 ± 9.64, P < 0.001) was significantly lower in the patients with SCF compared to the healthy controls with normal epicardial coronary arteries. Mean level of serum triglycerides (162.26 ± 45.94 vs. 145.29 ± 35.62, P < 0.001) was significantly higher in the patients with SCF. Left anterior descending artery was the most common involved coronary artery (n = 159, 92.4%), followed by left circumflex artery (n = 50, 29.1%) and right coronary artery (n = 47, 27.4%). Body mass index (BMI) (OR 1.78, 95% CI 1.04-2.25, P < 0.001) and hypertension (OR 1.59, 95% CI 1.30-5.67, P = 0.003) were independent predictors of SCF phenomenon.

Conclusion: The prevalence of SCF in our study was not different from the most other previous reports. BMI and hypertension independently predicted the presence of SCF phenomenon.
angiography at Imam Ali Cardiovascular Hospital affiliated with the Kermanshah University of Medical Sciences (KUMS), Kermanshah province, Iran from March 2016 to March 2018.

Materials and Methods
Study Population and Design
This cross-sectional study was performed at Imam Ali Cardiovascular Hospital, affiliated with KUMS, Kermanshah province, Iran. From March 20, 2017 to March 20, 2019, all the patients who underwent coronary angiography were assessed for inclusion in this study. Patients aged ≥18 years old presenting with normal epicardial coronary arteries (NECA) but having SCF on angiogram were selected (n=172). Also, patients aged ≥18 years old presenting with NECA and having normal flow on angiogram were selected (n=1848). SCF phenomenon is characterized by the delayed distal vessel opacification of contrast, in the absence of significant epicardial coronary stenosis. So that, in the patients with chest pain undergoing coronary angiography, actually, a delayed progression of the contrast material is found through epicardial coronary arteries without obstruction. Angiographic film should be prepared at a speed of 30 frames per second and contrast injection should be done by a 6F catheter to measure TFC. In the first frame, contrast material fully opacifies origin of the artery. The last frame is predefined for each coronary artery: so that, for the left anterior descending (LAD) and circumflex (Cx) arteries, it shows the most distal bifurcation, whereas for right coronary artery (RCA), it shows emergence of the first posterolateral (PL) branch. For LAD, apical segment is the milestone for TFC. Because, LAD is usually longer than the other arteries, a correction factor is required when calculating this score by dividing TFC of LAD by 1.7. Cut point of TFC was equal to 21 ± 2 for LAD, and it was equal to 22 ± 4 and 20 ± 3 for LCx and RCA, respectively. Patients who had coronary artery diseases (such as plaque, spasm, ectasia, stenosis, or obstructive lesion), and/or they had previously undergone coronary artery bypass grafting (CABG) or percutaneous coronary intervention (PCI), and/or they had embolism, heart failure, valvular heart disease, and connective tissue disorders, as well as those who were not resident in city of Kermanshah (living for less than 6 months), and those with incomplete personal or medical information, were excluded from the study.

Instruments and Data Collection
Data were collected by a nurse who was well trained in data collection using a checklist developed based on the study’s aims. He extracted the data from the patients’ medical records (including both paper and electronic medical records). The checklist was assessed and approved by obtaining experts’ opinions including a statistician and two cardiologists. All the checklists were checked and verified by a general physician who was responsible for quality control. The checklist was comprised of five following parts: demographic characteristics (e.g., gender), clinical histories (e.g., diabetes mellitus), laboratory parameters (e.g., C-reactive protein (CRP)), angiographic findings (e.g., culprit vessels), and electrocardiography data.

Results
A total of 11970 coronary angiographies were performed at Imam Ali Cardiovascular Hospital from March 2016 to March 2019, as a result of which 1848 (15.43%) patients with NECA and 172 (1.43%) patients with SCF phenomenon were identified. Demographic and clinical characteristics of the patients are reported in Table 1. Mean age of the patients with SCF was equal to 53.07 ± 9.81 years old, and for the patients with NECA, it was equal to 52.17 ± 10.84 years old (P = 0.256). Mean BMI was equal to 27.58 ± 3.28 for the patients with SCF vs. 24.12 ± 3.26 for the patients with NECA (P < 0.001). Prevalence rates of the current smoker (37.2% vs. 27.2%, P = 0.006), hypertension (53.5% vs. 39.1%, P < 0.001), and hypercholesterolemia (44.2% vs. 31.7, P < 0.001) were significantly higher in the patients with SCF compared to the patients with NECA. Of course, blood pressure of >139/89 mm Hg was defined as hypertension 10. Patients with NECA were more likely to have negative C-reactive protein (80.5% vs. 51.2%, P < 0.001). Comparing the lipid profiles, it was observed that, mean level of serum triglycerides (162.26 ± 45.94 vs. 145.29 ± 35.62, P < 0.001) was significantly higher in the patients with SCF compared to the patients with NECA. Mean EF (51.91 ± 6.33 vs. 55.15 ± 9.64, P < 0.001) was significantly lower in the patients with SCF compared to the patients with NECA. Out of 172 patients with SCF, 111 (64.5%) of them had stable angina, 49 (28.5%) of them had unstable angina, 5 (2.9%) of them had ST-segment elevation myocardial infarction (STEMI), 3 (1.7%) of them had non-STEMI, and 4 (2.3%) of them had ventricular tachycardia. Out of 172 patients with SCF, 98 (57.0%) of them had normal
electrocardiography, 69 (40.1%) of them presented ST-T change, and 5 (2.9%) of them presented STEMI.

Out of 172 patients with SCF, 100 (58.2%) of them had slow flow in 1 artery, 60 (34.9%) of them had slow flow in 2 arteries, and 12 (7.0%) of them had slow flow in all 3 arteries. The most common involved artery was LAD (n = 159, 92.4%), followed by LCx (n = 50, 29.1%) and RCA (n = 47, 27.4%) (Figure 1).

Mean TFC in LAD (39.60 ± 4.51 vs. 17.79 ± 2.84, \( P < 0.001 \)), LCx (40.41 ± 3.86 vs. 16.99 ± 1.83, \( P < 0.001 \)), and RCA (36.69 ± 3.31 vs. 18.69 ± 2.34, \( P < 0.001 \)) indicated slow flow phenomenon in the patients with SCF (Table 2).

Analysis of the results of multiple logistic regression identified BMI (OR 1.78, 95% CI 1.04-2.15, \( P = 0.003 \)) and hypertension (OR 1.59, CI 1.30-5.67, \( P = 0.003 \)) as independent predictors of SCF phenomenon (Table 3).

Discussion
This cross-sectional study was performed on the patients who underwent coronary angiography at Imam Ali Cardiovascular Hospital affiliated with KUMS, Kermanshah province, Iran from March 2017 to March 2019, to determine angiographic prevalence and clinical predictors of SCF phenomenon. To the best of our knowledge, the present study was the largest study particularly investigated clinical features of the patients with SCF phenomenon in an Iranian population in west of the country. Strength of the present study was its large sample size compared to the other studies assessing SCF phenomenon.

In our study, prevalence of SCF phenomenon was determined as 1.43%. Sanati et al, reported a prevalence of about 2% in a study from Iran in 2016.\(^{16}\) Hawkins et al in a study from Oklahoma, USA found a prevalence rate of 5.5% in the patients who underwent coronary angiography in 2012.\(^{17}\) Beltrame et al reported that 1% of all the patients who underwent coronary angiography had SCF phenomenon in Australia.\(^{4}\) In 2018, Mukhopadhyay

| Variable                  | SCF (n= 172) | NECA (n=1848) | \( P \) value |
|---------------------------|--------------|---------------|--------------|
| Age, y                    | 53.07 ± 9.81 | 52.17 ± 10.84 | 0.256*       |
| Body mass index, kg/m\(^2\) | 27.58 ± 3.28 | 24.12 ± 3.26  | <0.001*      |
| Male                      | 121 (70.3)   | 1310 (70.9)   | 0.882**      |
| Current smoker            | 64 (37.2)    | 503 (27.2)    | 0.006**      |
| Diabetes mellitus         | 53 (30.8)    | 470 (25.4)    | 0.123**      |
| Hypertension              | 92 (53.5)    | 723 (39.1)    | <0.001**     |
| Hypercholesterolemia      | 76 (44.2)    | 586 (31.7)    | <0.001**     |
| Hematocrit                | 45.69 ± 19.17| 46.89 ± 17.67 | 0.430*       |
| Platelet\(^6\)            | 222000.94 ± 62000.23 | 220000.89 ± 61000.67 | 0.686* |
| Erythrocyte sedimentation rate | 14.16 ± 9.91 | 13.69 ± 9.17  | 0.550*       |
| C-reactive protein        |              |               |              |
| Negative                  | 88 (51.2)    | 1488 (80.5)   |              |
| \( 1^* \)                 | 60 (34.9)    | 355 (19.2)    | <0.001***    |
| \( 2^* \)                 | 23 (13.4)    | 5 (0.3)       |              |
| \( 3^* \)                 | 1 (0.6)      | 0 (0)         |              |
| Low-density lipoprotein   | 118.89 ± 41.67| 116.87 ± 38.15| 0.541*       |
| High-density lipoprotein  | 44.36 ± 9.09 | 45.14 ± 9.83  | 0.286*       |
| Triglycerides             | 162.26 ± 45.94| 145.29 ± 35.62| <0.001*      |
| Ejection fraction         | 51.91 ± 6.33 | 55.15 ± 9.64  | <0.001*      |

Abbreviations: SCF, slow coronary flow; NECA, normal epicardial coronary arteries
Continuous variables expressed as mean ± SD, otherwise n (%)
*Independent samples t-test; ** Chi-square; *** Fisher exact test

Figure 1. Slow flow pattern (numbers of culprit vessels) in our study population (n = 172)
found that prevalence rate of SCF phenomenon was equal to 0.8% in India. The reasons for these subtle differences are not clearly known; however, discrepancy in atherosclerotic burdens and cardiovascular risk factors among different ethnic populations may clarify these differences. SCF phenomenon has been suggested as an early phase of atherosclerosis, and is manifested by micro vascular dysfunction. Finally, differences in ethnic background, atherosclerotic burdens, and related comorbidities of the studied populations might explain these discrepancies.

Our results demonstrated that the patients with SCF were more plausible to be obese, hyperlipidemic, hypertensive, and smoker. Ghaffari et al indicated that the patients with SCF were more plausible to be obese and active smoker. Sanghvi et al found a higher prevalence of hypertension, dyslipidemia, and smoking in the patients with SCF. Hawkins et al found that the patients with SCF were more obese. Sanati et al reported that the patients with SCF were more likely to be hypertensive compared to those with NECA. Moreover, our results showed that the most common involved artery was LAD with a rate of 92% followed by LCx and RCA. This result is in accordance with the findings of the study by Sanati et al who reported LAD as the most common involved artery, with a rate exceeding 90%. Our finding was also in line with a previous study by Sanghvi et al in which LAD (82.5%) was the most common involved artery followed by LCx artery (67.5%) and RCA (60%). Furthermore, Beltrame et al indicated LAD as the most common involved artery in 86% of the patients with SCF. The artery involvement reported in the present study varied from that of the other studies. Hawkins et al found that LAD, LCx, and RCA were involved in 67, 69, and 58% of the patients, respectively. The reason for this discrepancy is unknown, though it may be due to racial differences and technical errors.

Clinical presentation of SCF phenomenon is diverse ranging from stable or unstable angina and NSTEMI to STEMI. In the present study, 64.5% of the patients with SCF presented with stable angina and remaining of them (33.2%) presented with acute coronary syndrome (ACS) (28.5% with unstable angina, 2.9% with STEMI, and 1.7% with NSTEMI). Mukhopadhyay in a study from India in 2018 reported that 50% of the patients with SCF presented with stable angina and 50% of them presented with ACS (35% with unstable angina and 15% with NSTEMI). Likewise, in an earlier study done on Iranian population, it
was reported that 75% of the patients with SCF presented with ACS. 14 Sanghvi et al found that ACS (42.5%) was the most common clinical presentation in the patients with SCF.11 Beltrame et al reported that 75% of the patients with SCF phenomenon presented with ACS.1 Moreover, Yaron Arbel et al in a study from Israel reported that non-specific chest pain (71.9%), ACS (18.4%) and stable angina (8.8%) were among the most common presenting complaints in the patients with SCF, respectively.22

Our study had several limitations. Firstly, cross-sectional nature of the present study did not allow further evaluation of any apparent associations over time; hence for evaluating causality, longitudinal studies with an extended follow-up should be done. Secondly, our data were obtained from a single center; therefore, our participants may not be representative of the whole patients with SCF phenomenon. Moreover, the patients’ usage of medication was not reported in this study.

Conclusion
Our results showed that in the studied population, prevalence rate of SCF phenomenon was equal to 1.43%. Also, BMI and hypertension independently predicted the presence of SCF phenomenon. The most common involved artery was LAD followed by LCx and RCA. Majority of the patients with SCF presented with stable angina. Accordingly, further studies are needed to determine mechanisms of action of the mentioned predictors (BMI and hypertension). Finally, the current study provides a foundation for future studies that should be conducted in the other ethnic groups residing in different parts of Iran.

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Competing interest
The authors declare that they have no conflict of interest. In addition, the authors have no financial interest related to any aspect of the study.

Ethical approval
The study protocol and research process were approved and monitored by the Research Ethics Committee at KUMS (IR.KUMS.REC.1398.380). Moreover, the individual’s personal information was kept confidential with the access limited to researcher.

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