Clinical, Angiographic Characteristics and In-Hospital Outcomes of Smoker and Nonsmoker Patients After Primary Percutaneous Coronary Intervention

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ABSTRACT

Background: Smoking is a well-established cardiac risk factor there is dearth of Local data regarding clinical and angiographic characteristics of smoker patients.

Objectives: This study was planned to assess the differences in the clinical characteristics, angiographic characteristics, and in-hospital outcomes of smokers and nonsmokers after primary percutaneous coronary intervention at a tertiary care hospital in Karachi, Pakistan.

Methods: We included patients between 40 and 80 years of age diagnosed with ST-segment elevation myocardial infarction who underwent primary percutaneous coronary intervention from July 1, 2017, to March 31, 2018. Clinical and angiographic characteristics and in-hospital outcomes were obtained from the cases submitted to the National Cardiovascular Data Registry's CathPCI (Catheterization—Percutaneous Coronary Intervention) Registry from our site.

Results: A total of 3,255 patients were included in this study. Smokers consist of 25.1% (817) of the total sample. A high majority of smokers were male, 98.8% (807), and smokers were relatively younger as compared to nonsmokers with a mean age of 52.89 ± 10.59 versus 55.98 ± 11.24 years; $p < 0.001$. Smokers had higher post-procedure TIMI (Thrombolysis In Myocardial Infarction) flow grade III: 97.8% (794) versus 95.53% (2,329); $p = 0.037$, and they had a relatively low mortality rate: 2.69% (22) versus 3.16% (77); $p = 0.502$.

Conclusions: Smokers were predominantly male and around 3 years younger than nonsmokers. Diabetes mellitus and hypertension were less common among smokers and single-vessel disease was the more common angiographic finding for smokers as compared to 3-vessel disease for nonsmokers. No statistically significant differences in in-hospital outcomes were observed. ST-segment elevation myocardial infarction in smokers despite younger age and the low atherosclerotic risk profile, in our region, emphasize the need for nicotine addiction management and smoking cessation campaigns at large and for pre-discharge counseling.

With the current growth in the death toll, directly or indirectly, linked with tobacco use is expected to rise to 1 billion in the 21st century as against 100 million in the 20th century [1]. Tobacco use is a well-established cardiac risk factor associated with a rising risk of cardiovascular death or acute coronary syndrome [2–4]. A number of studies have confirmed its significant direct and persistent impact on cardiovascular health, even after making appropriate adjustments for other well-known risk factors [5–9]. Risk of myocardial infarction (MI) and sudden cardiac death attributable to smoking is 3× to 4× and around 10× higher, respectively [10,11]. An unexpected survival and prognostic benefit of smoking observed in patients with MI was termed as the "smoker's paradox." In later studies, this dubious phenomenon was attributed to the less extensive risk profile, low disease severity, and most importantly younger age. With an appropriate adjustment of these confounding factors, the dubious benefit of smoking diminished [12].

A longitudinal study on a middle-aged population-based cohort established an association between the progressions of atherosclerosis and active smoking [13]. Exact mechanisms and convoluted toxic components of smoking in the progression and development of cardiovascular dysfunction are mostly undefined, however, increase in oxidative stress due to cigarette smoking is among the

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TABLE 1. Comparisons of demographics, medical history, clinical presentation, angiographic characteristics, and post-procedural in-hospital complications and outcomes by smokers and nonsmokers

	Total	Nonsmokers	Smokers	
Variables	n = 3,255	n = 2,438	n = 817	p Value
Age, yrs	55.2 ± 11.16	55.98 ± 11.24	52.89 ± 10.59	<0.001*
Male	2,692 (82.7)	1,885 (77.32)	807 (98.78)	<0.001*
Female	563 (17.3)	553 (22.68)	10 (1.22)	<0.001*
Medical history				
Hypertension	1,421 (43.66)	1,130 (46.35)	291 (35.62)	<0.001*
Family history of CAD	118 (3.63)	82 (3.36)	36 (4.41)	0.167
Prior MI	216 (6.64)	164 (6.73)	52 (6.36)	0.718
Prior HF	14 (0.43)	9 (0.37)	5 (0.61)	0.358
Prior PCI	95 (2.92)	75 (3.08)	20 (2.45)	0.355
Diabetes	861 (26.45)	719 (29.49)	142 (17.38)	<0.001*
Anginal class				
No symptoms, no angina	1,505 (46.24)	1,134 (46.51)	371 (45.41)	0.584
CCS I	206 (6.33)	142 (5.82)	64 (7.83)	0.041*
CCS II	393 (12.07)	298 (12.22)	95 (11.63)	0.651
CCS III	596 (18.31)	445 (18.25)	151 (18.48)	0.883
CCS IV	555 (17.05)	419 (17.19)	136 (16.65)	0.722
Pre-procedure TIMI flow grade				
0	1,890 (58.06)	1,434 (58.82)	456 (55.81	0.131
1	334 (10.26)	251 (10.3)	83 (10.16)	0.911
2	625 (19.2)	466 (19.11)	159 (19.46)	0.827
3	406 (12.47)	287 (11.77)	119 (14.57)	0.036*
Number of diseased vessels				
None	27 (0.83)	19 (0.78)	8 (0.98)	0.585
SVD	1,057 (32.47)	743 (30.48)	314 (38.43)	<0.001*
2VD	919 (28.23)	704 (28.88)	215 (26.32)	0.159
3VD	752 (23.1)	597 (24.49)	155 (18.97)	0.001*
Data missing	500 (15.36)	375 (15.38)	125 (15.3)	0.955
Localization of culprit lesion				
LAD	1,766 (54.25)	1,321 (54.18)	445 (54.47)	0.887
RCA	1,084 (33.3)	811 (33.26)	273 (33.41)	0.937
LCX	348 (10.69)	261 (10.71)	87 (10.65)	0.963
PDA	28 (0.86)	24 (0.98)	4 (0.49)	0.185
Ramus	11 (0.34)	9 (0.37)	2 (0.24)	0.596
LM	18 (0.55)	12 (0.49)	6 (0.73)	<0.001*
Significant stenosis, >70%				
LM >50%	45 (1.38)	35 (1.44)	10 (1.22)	0.653
Prox LAD	1,223 (37.57)	926 (37.98)	297 (36.35)	0.405
Mid-distal LAD	1,557 (47.83)	1,182 (48.48)	375 (45.9)	0.2
LCX	1,308 (40.18)	1,017 (41.71)	291 (35.62)	0.002*
RCA	1,694 (52.04)	1,289 (52.87)	405 (49.57)	0.102
Ramus	91 (2.8)	69 (2.83)	22 (2.69)	0.836
Lesion complexity				
Nonhigh/nonC lesion	1,793 (55.08)	1,341 (55)	452 (55.32)	0.873
High/C lesion	1,462 (44.92)	1,097 (45)	365 (44.68)	0.873
Post-procedure TIMI flow grade				
0	25 (0.77)	20 (0.82)	5 (0.61)	0.554
1	27 (0.83)	20 (0.82)	7 (0.86)	0.92
2	80 (2.46)	69 (2.83)	11 (1.35)	0.017*
3	3,123 (95.94)	2,329 (95.53)	794 (97.18)	0.037*

(continued)

TABLE 1. Continued

Variables	Total n = 3,255	Nonsmokers n = 2,438	Smokers n = 817	p Value
In-hospital post-procedure outcomes				
Mortality	99 (3.04)	77 (3.16)	22 (2.69)	0.502
Reinfarction	17 (0.52)	10 (0.41)	7 (0.86)	0.125
Cardiogenic shock	43 (1.32)	32 (1.31)	11 (1.35)	0.941
HF	29 (0.89)	23 (0.94)	6 (0.73)	0.582
Cerebrovascular accident	3 (0.09)	3 (0.12)	0 (0)	0.315
Dialysis	5 (0.15)	4 (0.16)	1 (0.12)	0.792
Vascular complications	1 (0.03)	1 (0.04)	0 (0%)	0.562
Transfusion	3 (0.09)	2 (0.08)	1 (0.12)	0.742
Bleeding	19 (0.58)	17 (0.7)	2 (0.24)	0.141

Values are mean ± SD or n (%). The p values are computed based on chi-square test or Mann-Whitney *U* test.
CAD, coronary artery disease; CCS, Canadian Cardiovascular Society; HF, heart failure; LAD, left anterior descending; LCX, left circumflex artery; LM, left main artery; MI, myocardial infarction; PCI, percutaneous coronary intervention; PDA, pulmonary descending artery; Prox, proximal; RCA, right coronary artery; SVD (2VD, 3VD), single- (2-, 3-) vessel disease; TIMI, Thrombolysis In Myocardial Infarction.
*Significant at 5%.

clinically and experimentally supported hypotheses for the progression of cardiovascular dysfunction [14]. Alongside its direct impact, smoking has also indirect influence on cardiovascular health and its multiplicative interaction with other well-established cardiovascular risk factors, such as low levels of high-density lipoprotein cholesterol, glucose intolerance or diabetes mellitus, and untreated hypertension, as evident from past studies [5].

Angiographic assessment is a vital step in the planning management and treatment for patients with cardiovascular diseases. Local data regarding clinical and angiographic characteristics of smoker patients is lacking. This study was planned to assess the differences in the clinical characteristics, angiographic characteristics, and in-hospital outcomes of smokers and nonsmokers after primary percutaneous coronary intervention (PCI) at a tertiary care hospital in Karachi, Pakistan.

METHODS

After institutional approval, data for this study were obtained from the cases submitted to the National Cardiovascular Data Registry's CathPCI (Catheterization Percutaneous Coronary Intervention) Registry from the site National Institute of Cardiovascular Diseases, Karachi, Pakistan, from July 1, 2017, to March 31, 2018. Inclusion criteria for the study were patients of either sex, diagnosed with ST-segment elevation myocardial infarction (STEMI), undergoing primary PCI, and age between 40 and 80 years. Primary PCI was classified as the procedure within 24 h after subsequent electrocardiographic findings of STEMI. Candidacy of the patients for the PCI procedure was assessed and all the contraindications for the PCI were ruled out, and all the angiographic and PCI procedures were performed by the experienced (more than 5 years) intervention cardiologists.

Data were categorized into 2 groups—smokers, and nonsmokers—and as per the National Cardiovascular Data Registry definition, smokers were defined as the patients with a history of smoking cigarettes during 1-year period of hospital arrival. Data regarding demographics, medical history, clinical presentation, angiographic characteristics, and post-procedural in-hospital complications and outcomes were obtained and comparison was made between the smoker and nonsmoker groups. Post-procedure in-hospital outcomes include all-cause mortality, reinfarction (clinically diagnosed new MI during post-procedure hospital stay based on signs and symptoms), cardiogenic shock (new onset or recurrence of cardiogenic shock with hemodynamic compromise persisted for more than 30 min), heart failure (physician-documented acute recurrence or new-onset heart failure), cerebrovascular accident or stroke (clinically diagnosed neurologic dysfunction observed during hospital stay), dialysis (renal dialysis required due to worsening or acute renal failure during hospital stay), and event of suspected bleeding (either hemoglobin dropped by ≥3 g/dl or needed transfusion), and other vascular complications.

IBM SPSS Statistics for Windows version 21.0(IBM Corp., Armonk, New York) was used for the analysis of extracted data. All the continuous variables, such as age in years and left ventricular ejection fraction (%), were assessed for the normality of the distribution by applying Kolmogorov-Smirnov test and appropriate independent sample Student's *t*-test or Mann-Whitney *U* test was applied for the comparison between the groups. Responses on categorical response variables were dichotomized and comparison was made by applying chi-square test, and binary logistic regression was performed for univariate and multivariate analysis. Significant variables on univariate analysis and other clinically significant variables such as sex, hypertension, diabetes, smoking, positive family

TABLE 2. Determinants of in-hospital mortality

	Univariate		Multivariate	
Characteristics	OR (95% CI)	p Value	OR (95% CI)	p Value
Age, yrs	1.02 (1–1.04)	0.017*	1.02 (1–1.04)	0.064
Male	0.72 (0.45–1.17)	0.19	0.75 (0.45–1.27)	0.288
Hypertension	1.22 (0.82–1.82)	0.326	0.99 (0.64–1.52)	0.958
Diabetes	1.41 (0.92–2.15)	0.117	1.24 (0.79–1.95)	0.348
Smoking	0.85 (0.52–1.37)	0.503	1.07 (0.64–1.78)	0.792
Positive family history	0.27 (0.04–1.92)	0.188	0.28 (0.04–2.06)	0.212
Prior MI	1.25 (0.6–2.6)	0.558	1.22 (0.57–2.58)	0.611
Prior PCI	0.68 (0.16–2.8)	0.592	—	—
CCS class III or IV	0.95 (0.63–1.45)	0.83	—	—
Pre-procedure TIMI flow grade 0 to I	2.13 (1.27–3.56)	0.004*	2.35 (1.38–4.01)	0.002*
Multivessel disease	2.38 (1.49–3.78)	<0.001*	2.28 (1.42–3.68)	<0.001*
Culprit LAD	1.49 (0.99–2.26)	0.059	—	—
Culprit RCA	0.6 (0.37–0.96)	0.033*	0.52 (0.32–0.85)	0.008*
Culprit LCX	0.94 (0.48–1.82)	0.847	—	—
Culprit LM	6.54 (1.86–22.98)	0.003*	10.09 (2.64–38.57)	<0.001*
High/C lesions	1.49 (1–2.23)	0.052	1.02 (1–1.04)	0.064

CI, confidence interval; OR, odds ratio; other abbreviations as in Table 1.

*Significant at 5% level of significance.

history, and prior MI were used as explanatory variables for the multivariate analysis. A p value of ≤0.05 for the differences between smoker and nonsmoker groups was considered statistically significant.

RESULTS

A total of 3,255 patients diagnosed with STEMI who underwent immediate PCI were included in this study. Smokers are 25.1% (817) of the total sample. A high majority of smokers were male, 98.8% (807), and smokers were relatively younger than nonsmokers with a mean age of 52.89 ± 10.59 versus 55.98 ± 11.24 years; $p < 0.001$. Diabetes was more common among nonsmokers: 29.5% (719) versus 17.4% (142); $p < 0.001$. Similarly, smokers were observed to be less hypertensive than nonsmokers: 35.6% (291) versus 46.4% (1,130); $p < 0.001$. Proportion of patients with pre-procedure TIMI (Thrombolysis In Myocardial Infarction) flow grade III was significantly higher among smokers: 14.6% (119) versus 11.8% (287); $p = 0.036$.

Significantly higher proportion of smokers had single-vessel diseased: 38.4% (314) versus 30.5% (743); $p < 0.001$; whereas, significantly higher number of nonsmokers had 3-vessel disease: 24.5% (597) versus 19.0% (155); $p = 0.001$. Significant stenosis (>70%) in the left circumflex artery was observed in significantly more nonsmokers than smokers: 41.7% (1,017) versus 35.6% (291); $p = 0.002$. However, no significant differences were observed between smoker and nonsmoker groups in terms of localization of culprit lesion other than left main involvement, which was found to be significantly higher in the smoker group: 0.73% (6) versus 0.49% (12); $p < 0.001$. Comparisons of demographics, medical history, clinical presentation, angiographic characteristics, and post-procedural in-hospital complications and outcomes by smokers and nonsmokers are presented in Table 1.

Univariate and multivariate analysis to identify the determinants of in-hospital mortality are presented in Table 2. The independent predictors of in-hospital mortality were found to be pre-procedure TIMI flow grade of 0 to I, multivessel disease, and culprit left main with an adjusted odds ratio of 2.35 (95% confidence interval [CI]: 1.38 to 4.01), 2.28 (95% CI: 1.42 to 3.68), and 10.09 (95% CI: 2.64 to 38.57), respectively. Smoking status was found to have associated with increased mortality however, the association was found to be insignificant with an unadjusted odds ratio of 1.07 (95% CI: 0.64 to 1.78).

DISCUSSION

To the best of our knowledge, this is the largest study from Pakistan with an extensive dataset of 3,255 patients who had undergone primary PCI for STEMI. We observed various disparities among smokers and nonsmokers in terms of risk profile and angiographic characteristics and in-hospital outcome.

In our study, the smokers group consisted of significantly younger patients with a mean age of 52.89 ± 10.59 years versus 55.98 ± 11.24 years in the nonsmoker group. These findings are aligned with those of past studies addressing smoker and nonsmoker disparities that smokers are significantly younger than nonsmokers [11,15–25]. However, the magnitude of the age difference between

TABLE 3. Comparative findings in smokers and nonsmokers reported in past studies

Characteristic	Author Ref. #	Smokers vs. Nonsmokers	p Value
Age, yrs	Gupta et al. [11]	51.6 ± 13.8 vs. 59.5 ± 11.6	<0.001*
	Shemirani et al. [23]	53.5 ± 10.6 vs. 61.5 ± 10.6	<0.001*
	Rakowski et al. [16]	56 (48–65) vs. 68 (60–76)	<0.001*
	Goto et al. [19]	55 (49–62) vs. 66 (57–74)	<0.001*
	Symons et al. [22]	55.3 ± 9.9 vs. 64.4 ± 11.3	<0.001*
	Katayama et al. [24]	64 ± 11 vs. 74 ± 10	<0.001*
	Haig et al. [25]	55 ± 11 vs. 65 ± 10	0.001*
Female	Gupta et al. [11]	1.1 vs. 43.3	<0.001*
	Shemirani et al. [23]	4.3 vs. 25.5	<0.001*
	Rakowski et al. [16]	18.4 vs. 28.8	<0.001*
	Goto et al. [19]	20.3 vs. 24.9	0.002*
	Symons et al. [22]	14.1 vs. 20.1	0.09
	Katayama et al. [24]	9.1 vs. 50.0	<0.001*
	Haig et al. [25]	29.1 vs. 23.4	0.305
Hypertension	Gupta et al. [11]	14.4 vs. 46.7	<0.001*
	Shemirani et al. [23]	15.2 vs. 44.7	0.001*
	Goto et al. [19]	44.5 vs. 60.1	0.001*
	Symons et al. [22]	42.3 vs. 48.8	0.16
	Katayama et al. [24]	43.1 vs. 41.9	0.779
	Haig et al. [25]	26.5 vs. 41.4	0.007*
Diabetes mellitus	Gupta et al. [11]	32.2 vs. 61.7	<0.001*
	Shemirani et al. [23]	17.0 vs. 36.2	0.02*
	Rakowski et al. [16]	10.0 vs. 18.6	<0.001*
	Goto et al. [19]	12.5 vs. 19.7	0.001*
	Symons et al. [22]	11.0 vs. 18.4	0.02*
	Katayama et al. [24]	31.0 vs. 37.2	0.141
	Haig et al. [25]	10.2 vs. 10.9	0.854
Multivessel disease	Rakowski et al. [16]	45.1 vs. 54.9	0.001*
	Goto et al. [19]	0 vs. 0	0.001*
	Katayama et al. [24]	37.9 vs. 45.9	0.064
	Haig et al. [25]	43.9 vs. 50.0	<0.001*
Mortality, 24 h	Shemirani et al. [23]	4.3 vs. 6.4	0.72
Mortality, 30 days	Gupta et al. [11]	7.8 vs. 3.3	<0.001*
	Rakowski et al. [16]	2.3 vs. 6.6	0.002*
	Goto et al. [19]	1.3 vs. 3.3	<0.001*
Mortality, 6 months	Katayama et al. [24]	3.0 vs. 9.1	0.01*

Values are mean ± SD, or percentage.
*Significant at 5%.

smokers and nonsmokers in our study was around 3 years (55.98 to 52.89), whereas around 8 to 12 years of the age difference between the smoker and nonsmoker groups was observed in past studies (see Table 3) [11,16,19,22–25]. This narrowing difference in age, between smokers and nonsmokers, in our population, is alarming and a possible indication of early-onset MI in our population. Further studies are needed to understand this phenomenon.

In general, the smoking tendency among women in our population is less than in other populations. Only 1.2% (10) of the smoker group consisted of women, which is a consistent finding: in Gupta et al. [11], it is 1.1%; Shemirani et al. [23], 4.26%; and Katayama et al. [24], 9.1%. However, the proportion of women in the smoker groups reported in some other populations was around 14% to 29% [16,19,22,25].

Clinical presentation (Canadian Cardiovascular Society anginal classification) for both smokers and nonsmokers was similar in our study, with similar phenomena that have been reported in the past studies [11,16,25]. Similarly, diabetes and hypertension were less prevalent among smokers than nonsmokers, this is a consistent finding among various studies from other parts of the world [11,15,16,18–29].

We found a similar distribution of culprit arteries in the smoker and nonsmoker groups, which was consistent with some of the past studies [11,22–25]. But Rakowski et al. [16] and Goto et al. [19] reported

involvement of the left anterior descending artery was more common for nonsmokers and the right coronary and left circumflex arteries were more commonly observed in smokers.

In our study, multivessel disease ([MVD]; 2 or 3 vessels) was significantly higher among nonsmokers (53.36% vs. 45.29%; $p < 0.001$) and single-vessel disease was observed in a significantly higher number in the smoker group (38.43% vs. 30.48%; $p < 0.001$). A similar distribution of diseased vessels was reported by Rakowski et al. [16]. They reported MVD in 54.9% versus 45.1%; $p = 0.001$, of nonsmokers and smokers, respectively. Haig et al. [25] also reported a significantly higher number of nonsmokers than smokers with MVD: 43.9% versus 50.0%; $p < 0.001$. Similarly, a significantly higher rate of severe coronary anatomy (MVD) among nonsmokers was observed by other studies [15,18,24,26,29].

Post-procedure in-hospital outcomes were relatively better in the smoker group with higher ratio of post-procedure TIMI flow grade III (97.8% vs. 95.53%), low mortality rate (2.69% vs. 3.16%), and low rate of other significant adverse outcomes, such as reinfarction, cardiogenic shock, cerebrovascular accident, and bleeding. Our observation of comparatively better outcomes among smokers is same as other studies [12,15,16,19–21,23,24,27–29]. The published reports are filled with various explanations for this dubious beneficial impact of smoking in acute MI. In our study, this can be attributed to the low atherosclerotic risk profile of the smoker group with relatively younger age, lesser prevalence of diabetes and hypertension, and less severe coronary anatomy (MVD). It has been reported that with an appropriate adjustment of these confounding factors, the dubious benefit of smoking diminishes [12], and studies have reported poor post–coronary revascularization follow-up in smokers [12,18,25,28,30].

Study Limitations

Despite being the largest study in our population, this study has several limitations. It is a single-center retrospective study conducted on data from a prospectively collected registry. Therefore, the impact of duration of smoking, type of tobacco, and the number of cigarettes could not be established. Also, only in-hospital outcomes were available. Prospective studies with long-term follow-up are needed.

CONCLUSIONS

There is a deficiency of data from the South Asian region regarding the disparities between smokers and nonsmokers. Comparative assessment of smoker and nonsmoker patients treated with primary PCI for STEMI showed that the smokers were predominantly male and around 3 years younger than nonsmokers. Diabetes mellitus and hypertension were less common among smokers and single-vessel disease was the more common angiographic finding for smokers and 3-vessel disease for nonsmokers. However, no statistically significant differences in in-hospital outcomes were observed, therefore, it is imperative to elaborate the role of smoking in the progression of cardiovascular disease and its impact on hospital course of the patients in this population. STEMI in smokers despite younger age and the low atherosclerotic risk profile, in our region, emphasizes the need for nicotine addiction management and smoking cessation campaigns at large and for pre-discharge counseling.

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