

Letters

RESEARCH LETTER

Comparison of Premature, Extremely Premature, and Older Adults With Coronary Artery Disease in Pakistan



With recent developments in noninvasive imaging and pharmacological interventions (statins), the prevalence of premature coronary artery disease (CAD) in developed countries has declined over the last 2 decades, yet the number of years lost to premature CAD in developing countries contributes >80% to the global burden of this disease.¹ We assessed the prevalence of risk factors and outcomes of percutaneous cutaneous coronary intervention (PCI) in patients with premature and extremely premature CAD in Pakistan.

Data were obtained from the Cardiac Registry of Pakistan Catheterization Percutaneous Coronary Intervention 2016 to 2019, which is a registry of consecutive patients. Patients were divided into 3 groups: older (men >55 years of age, women >65 years of age), premature (men 40-54 years of age, women 40-64 years of age), and extremely premature (<40 years of age) patients with CAD undergoing PCI. Standard National Cardiovascular Data Registry definitions were used to identify patients with ST-segment elevation myocardial infarction and non-ST-segment elevation myocardial infarction (NSTEMI). Categorical variables were compared using the chi-square and Fisher exact tests (for cell count <5). The median and IQR were compared using the Kruskal-Wallis test.

A total of 15,106 patients (6,041 [40.0%] older, 7,947 [52.6%] premature, and 1,118 [7.4%] extremely premature CAD patients undergoing PCI) were included. The proportion of missing values was <0.1%. The mean ages of older, premature, and

extremely premature patients were 64.8 ± 6.7 years, 50.3 ± 5.9 years, and 34.9 ± 3.7 years, respectively. The premature group had a significantly higher proportion of female patients (27.8% vs 10.1%), a greater prevalence of smoking (31.1% vs 28.1%), and a greater family history of premature CAD (17.9% vs 11.8%) compared with older adults with CAD. Similar trends were observed when comparing patients with extremely premature CAD with older adults with CAD.

The predominant clinical presentation of clinically significant CAD among premature and extremely premature groups was congestive heart failure (22.6% and 29.4%, respectively), and the indication for PCI was NSTEMI (51.6% and 56.7%, respectively). Compared with older adults, the overall risk of procedural and postprocedural complications of PCI in patients with premature CAD was rare (<2%), and survival was favorable (Table 1). On the contrary, post-PCI referral to cardiac rehabilitation centers was significantly lower in the premature (42.4%) and extremely premature (32.4%) CAD patients compared with the older adults with CAD (51.6%) ($P < 0.01$).

Our results show that female patients constituted a higher proportion of patients with premature CAD. This could partly be attributed to the lower age cutoff in the definition of CAD for the younger population and also to the higher incidence of obesity and accumulation of multiple risk factors in female patients.¹ Family history of premature CAD might explain the genetic basis of CAD or it may reflect clustering of poor lifestyle and traditional risk factors in families, increasing their risk of premature CAD in developing countries such as Pakistan.

In our study, the most common presentation (congestive heart failure) due to NSTEMI indicates that younger patients are equally vulnerable to ischemic events, albeit with a different presentation. The relatively better in-hospital outcomes and higher survival at the time of index PCI in the premature and extremely premature groups indicate that lower age serves as a strong inverse predictor of in-hospital mortality. This could also be linked to the relatively higher utilization of antiplatelet and statins medication in the younger cohort; however, the overall proportion of medication use was very low (~70%)

TABLE 1 Baseline and Procedural Characteristics, Clinical Presentation, and PCI Outcomes in Comparison Groups

	Group A: Older Adults With CAD (n = 6,041)	Group B: Premature CAD (n = 7,947)	Group C: Extremely Premature CAD (n = 1,118)	P Value		
				Comparing All 3 Groups	Comparing Groups A and B	Comparing Groups B and C
Sex and comorbidities						
Female	611 (10.1)	2,212 (27.8)	133 (11.9)	<0.01	<0.01	<0.01
Tobacco use (ever)	1,698 (28.1)	2,471 (31.1)	514 (46.0)	<0.01	<0.01	<0.01
Hypertension	3,837 (63.5)	4,702 (59.2)	468 (41.9)	<0.01	<0.01	<0.01
Family history of premature CAD	715 (11.8)	1,421 (17.9)	258 (23.1)	<0.01	<0.01	<0.01
Diabetes mellitus	2,295 (38.0)	2,891 (36.4)	232 (20.8)	<0.01	0.05	<0.01
Peripheral arterial disease	84 (1.4)	73 (0.9)	9 (0.8)	0.02	0.01	0.70
Prior myocardial infarction	1,404 (23.2)	2,158 (27.2)	344 (30.8)	<0.01	<0.01	0.01
Outcomes						
Coronary complications (dissection, perforation)	142 (2.4)	145 (1.8)	19 (1.7)	0.06	0.03	0.54
Cardiac arrest during or after PCI	42 (0.7)	37 (0.5)	2 (0.9)	0.04	0.07	0.22
Need for CABG during or after PCI	44 (0.7)	26 (0.3)	2 (0.2)	<0.01	<0.01	0.40
Cardiogenic shock during or after PCI	86 (1.4)	58 (0.7)	5 (0.5)	<0.01	<0.01	0.29
Stent thrombosis	8 (0.1)	10 (0.1)	3 (0.3)	0.43	0.91	0.24
Cardiac tamponade	3 (0.05)	3 (0.04)	0 (0.0)	1.00	1.00	1.00
Bleeding in 72 h of the PCI	31 (0.7)	25 (0.3)	1 (0.2)	0.05	0.07	0.36
Mortality during or after PCI	111 (1.8)	67 (0.8)	4 (0.4)	<0.01	<0.01	0.10
Cardiac rehabilitation referral	3,117 (51.6)	3,372 (42.4)	362 (32.4)	<0.01	<0.01	<0.01

Values are n (%).
 CABG = coronary artery bypass grafting; CAD = coronary artery disease; PCI = percutaneous coronary intervention.

compared with the developed countries. Together, these findings indicate that there is an unmet need to increase public awareness and medication compliance and ensure the implementation of primary prevention strategies in developing countries.

Our study has limitations. Due to variability in data reporting, we could not gather data on the severity of disease, door-to-balloon time, staged PCI, intravascular imaging, or post-PCI medication use. Similarly, long-term outcomes were also not available in these patients.

Tobacco smoking and the female sex were more prevalent in patients with premature and extremely premature CAD in Pakistan. PCI has favorable outcomes in these patients. A higher burden of modifiable risk factors and medication noncompliance coupled with lower rates of cardiac rehabilitation referral post-PCI identify the importance of early screening for risk factors, the need for increased awareness, and cardiac rehabilitation referral among young patients with CAD in the South Asian context.

Waqas Ullah, MD
 Rehan Malik, DPH
 Faiza Bashir, MBBS
 Mustafa Khan, MBBS

Saud Khan, MBBS
 Mahboob Alam, MD
 Zainab Samad, MBBS
 Miguel C. Achirica, MD
 Salim S. Virani, MD, PhD
 *Bashir Hanif, MD
 *Tabba Heart Institute
 Street 01, Block 02, Federal B Area
 Karachi 75950, Pakistan
 E-mail: bashir.hanif@tabbaheart.org
 Twitter: [@vakasullah](https://twitter.com/vakasullah)
<https://doi.org/10.1016/j.jacasi.2022.10.002>

© 2023 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

This study was exempted from the approval of the Institutional Review Board/ethics committee, as the data were de-identified. Dr Virani has received grant support from the Department of Veterans Affairs, the World Heart Federation, and the Tahir and Joona Family; and honoraria from the American College of Cardiology (Associate Editor for *Innovations*). All other authors have reported that they have no relationships relevant to the contents of this paper to disclose. The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the [Author Center](#).

REFERENCE

1. Rallidis LS, Xenogiannis I, Brilakis ES, et al. Angiographic characteristics, and management of premature myocardial infarction: JACC State-of-the-Art Review. *J Am Coll Cardiol.* 2022;79(24):2431-2449.