

## Original Research Article

# One year prognosis of young Middle Eastern patients undergoing percutaneous coronary interventions

Zayd I. Alhaddad<sup>1</sup>, Rawan A. Hammoudeh<sup>2</sup>, Rinad R. Tabbalat<sup>2</sup>,  
Yousef Khader<sup>3</sup>, Imad A. Alhaddad<sup>4</sup>, Ayman J. Hammoudeh<sup>5\*</sup>

<sup>1</sup>Imperial College Medical School, London SW7 2AZ, UK

<sup>2</sup>Department of Internal Medicine, Istishari Hospital, Amman 11954, Jordan

<sup>3</sup>Jordan University of Science and Technology, School of Allied Medical Sciences, Irbid 22110, Jordan

<sup>4</sup>Department of Cardiology, Jordan Hospital Medical Center, Amman 11152, Jordan

<sup>5</sup>Interventional Cardiology Service, Cardiology Department, Istishari Hospital, Amman 11954, Jordan

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### \*Correspondence:

Dr. Ayman J. Hammoudeh,

E-mail: Hammoudeh\_ayman@yahoo.com

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## ABSTRACT

**Background:** There is scarcity of data about the outcome in young Middle Eastern patients who undergo percutaneous coronary intervention (PCI). We sought to assess clinical and coronary angiographic features and one year outcome of young compared with older patients following PCI.

**Methods:** Baseline clinical and coronary angiographic features and major cardiovascular events from hospital admission to one year were assessed in young patients (<45 years of age) compared with older patients (>45 years of age).

**Results:** Of 2426 patients; 308 (12.7%) were young. Young and older patients were predominantly males (76.3% vs. 79.8%;  $p=0.18$ ) and had similar prevalence of hypertension, diabetes, dyslipidemia, and cigarette smoking. There were no differences between young and older patients in the rates of acute coronary syndrome as an indication for PCI (75.6% vs. 76.1%;  $p=0.90$ ). The two groups had similar prevalence of one-vessel coronary artery disease (55.2% vs. 58.1%;  $p=0.37$ ) and intervention for one vessel (74.0% vs. 72.1%;  $p=0.53$ ). No significant differences were observed in the incidence of in-hospital adverse events in young compared with older patients. Incidence of adverse events in young patients at one year were not different from those in older patients, including cardiac death (3.63% vs. 2.11%), stent thrombosis (3.63% vs. 2.08%), major bleeding (1.30% vs. 1.18%), and coronary revascularization (3.65% vs. 3.24%); all  $p=NS$ .

**Conclusions:** Among Middle Eastern patients undergoing coronary intervention; 13% were 45 years of age or younger. No favourable risk profile, coronary angiographic features or cardiovascular outcome were observed in young compared with older patients.

**Keywords:** Cardiovascular disease in the Middle East, Cardiovascular disease in the young, Percutaneous coronary intervention

## INTRODUCTION

Cardiovascular disease is the leading cause of death in the Middle East.<sup>1,2</sup> Patients admitted with acute coronary syndrome (ACS) are 7-10 years younger than their counterparts in the west, and about 20-25% are younger

than 45-50 years of age.<sup>3,4</sup> ACS has a significant socioeconomic impact on young patients, their families and the society as a whole, especially where the young constitute a significant percentage of the population, as it is the case in the Middle East.<sup>5-7</sup> An unsubstantiated notion that is frequently quoted by local and regional

healthcare providers implies that young patients are prone to excess adverse cardiovascular mortality and morbidity when they sustain ACS or undergo PCI compared with older patients.

There is scarcity of studies that address the cardiovascular risk profile, clinical presentations, coronary angiographic findings and prognosis (in-hospital and one year) in consecutive young Middle Eastern patients who are admitted with ACS or stable coronary disease and undergo percutaneous coronary intervention (PCI).

The large regional ACS registries elaborated on the patients populations as a whole, but specific data about the coronary angiographic features and one year outcome in young subgroups have not been published.<sup>1-7</sup> We, therefore, assessed these features and outcomes in the young subgroups of patients enrolled in a large prospective registry.

## METHODS

The study population consisted of 2426 patients who were consecutively enrolled in the first Jordanian PCI registry (JoPCR1). All patients underwent PCI for ACS or stable coronary disease in 12 tertiary care centers from January 2013 through February 2014, and were followed up for one year.

The clinical, electrocardiographic (EKG), echocardiographic and coronary angiographic features in patients 45 years of age or younger were compared with those of patients older than 45 years of age. The PCI indications and complications, and cardiovascular events during hospitalization and at one year of follow up were compared in the two groups.

A case report form was used to record patients' data prospectively during index hospitalization, and at 1,6, and 12 months of follow-up. Data were collected during follow-up visits or through phone calls to the patients, their household relative or primary care physicians.

All PCI procedures were performed according to current standard guidelines. The arterial access site, dual antiplatelet therapy, and type of stent, were left to operator's discretion. ACS was classified as acute ST-segment elevation myocardial infarction (STEMI), or non-ST-segment elevation ACS (NSTEMI). The latter included non-ST-segment elevation MI (NSTEMI), and unstable angina (UA).

Stable coronary disease included chronic stable angina and silent ischemia. The major cardiovascular events included cardiac deaths (all deaths were considered cardiac unless a definite non-cardiac cause could be established), definite and probable stent thrombosis (ST) as defined by the Academic Research Consortium, major bleeding events were defined according to the

CRUSADE study classification and included intracranial hemorrhage, retroperitoneal bleeding, hematocrit (Hct) drop >12% from baseline, any red blood cell (RBC) transfusion when baseline Hct was >28%, or any RBC transfusion when baseline was <28% with witnessed bleeding, and re-admission for ACS, heart failure or target vessel/lesion revascularization.<sup>8,9</sup>

Each patient signed an informed consent and the study was approved by the Institutional Review Board of each participating hospital.

## Statistical analysis

Data were described and analyzed using the IBM SPSS Statistics (version 20). Data were described using means, standard deviations, or percentages wherever appropriate.

The differences in the demographic and clinical characteristics and cardiovascular events during hospitalization, 1 month, 12 months between young and older patients were tested using chi-square test. Binary logistic regression models were developed for each cardiovascular event to adjust for important factors. A p-value of less than 0.05 was considered statistically significant.

## RESULTS

There were 308 young patients (12.7%) in the study. Table 1 depicts the baseline clinical characteristics and risk profiles of these patients compared with older patients. Young patients did not have statistically significant higher prevalence of major cardiovascular risk factors, especially hypertension, diabetes mellitus (DM), cigarette smoking and dyslipidemia compared with older patients.

This finding was reflected by similar rates of use of cardiovascular medications prior to admission in the two age groups. EKG, echocardiographic, coronary angiographic and percutaneous coronary intervention indications are shown in Table 2.

The prevalence rates of STEMI and elevated serum cardiac biomarkers in young patients were similar to those in older patients. The prevalence rates of multivessel coronary artery disease (CAD) and multivessel PCI were also similar in the two groups. Cardiovascular events during hospitalization and at 1 and 12 months are shown in Tables 3 and 4.

During the index hospitalization young patients did not have lower incidence rate of major life-threatening peri-procedural complications or cardiac mortality. The incidence of cardiovascular events at 1 and 12 months were not significantly different between young and older patients after adjusting for important predictors in multivariate logistic regression analysis.

At one year, there were 44 deaths in the whole cohort, including 11 (3.6%) in the young group and 44 (2.1%) in

the older group. The difference, however, was not statistically significant.

**Table 1: Baseline clinical features of patients who underwent percutaneous coronary intervention according to age.**

Clinical feature	Young patients (age ≤ 45 years old) N = 308 n (%)	Older patients (age ≤ 45 years old) N =2118 n (%)	P-value
Age (years) mean+SD	40.4+9.0	61.1+10.2	0.001
Men	235 (76.3)	1690 (79.8)	0.18
Hypertension	192 (62.3)	1304 (61.6)	0.86
Dyslipidemia	162 (52.6)	1027 (48.5)	0.20
Diabetes mellitus	172 (55.8)	1121 (52.9)	0.37
Family history of premature CVD	125 (40.6)	864 (40.8)	0.10
Current cigarette smoking	141 (45.8)	927 (43.8)	0.55
Past history of MI	82 (26.6)	529 (25.0)	0.59
Previous PCI	88 (27.6)	524 (24.7)	0.30
Medications upon admission:			
- aspirin	190 (61.7)	1356 (64.0)	0.47
- second oral antiplatelet agent (ticagrelor or clopidogrel)	59 (19.2)	442 (20.9)	0.54
- statin	158 (51.3)	1093 (51.6)	0.97
- beta blocker	148 (48.1)	996 (47.0)	0.76
- renin angiotensin system blocker	131 (42.5)	851 (40.2)	0.52

CVD: cardiovascular disease, MI: myocardial infarction; PCI: percutaneous coronary intervention

**Table 2: Electrocardiographic and coronary angiographic features and use of medications in young and older patients who underwent percutaneous coronary intervention.**

Feature	Young patients (age ≤ 45 years old) N = 308 n (%)	Older patients (age ≤ 45 years old) N =2118 n (%)	P-value
Electrocardiogram at presentation:			
- ST- segment elevation	87 (28.2)	664 (31.4)	0.26
- ST- segment depression	57 (18.5)	396 (18.7)	0.10
Elevated serum cardiac biomarkers	126 (40.1)	869 (41.0)	0.81
Left ventricular ejection fraction <45%	27 (8.8)	255 (12.0)	0.13
Heart failure on admission	27 (8.8)	232 (11.0)	0.29
Indication for PCI:			0.90
- Acute coronary syndrome:	233 (75.6)	1611 (76.1)	
- STEMI	82 (26.6)	653 (30.8)	
- NSTEMI	40 (13.0)	272 (12.8)	
- UA	111 (36.0)	686 (32.4)	
- Stable coronary disease	75 (24.4)	507 (23.9)	
Number of diseased of coronary arteries:			0.66
- single vessel	170 (55.2)	1231 (58.1)	
- two vessels	98 (31.8)	631 (29.8)	
- three vessels or more	40 (13.0)	256 (12.1)	
Number of coronary arteries treated by PCI:			0.17
- single vessel	228 (74.0)	1528 (72.1)	
- two vessels	73 (23.7)	492 (23.2)	
- three or more	7 (2.3)	98 (4.6)	
Medications during hospitalization:			
- Aspirin	306 (99.4)	2099 (99.1)	0.84
- Second oral antiplatelet agent (ticagrelor,	305 (99.0)	2111 (99.7)	0.18

clopidogrel)			
- Glycoprotein IIb/IIIa inhibitors	58 (18.8)	303 (14.3)	0.05
- Thrombolytic agent	4 (1.3)	66 (3.1)	0.11
- Statin	249 (80.8)	1995 (95.2)	<0.001
- Beta blocker	235 (76.3)	1565 (73.9)	0.41
- Renin angiotensin system blocker	176 (57.1)	1190 (56.2)	0.81
Medications at 1 year:			
- Aspirin	296 (99.0)	2006 (98.2)	0.11
- Second oral antiplatelet agent (ticagrelor, clopidogrel)	279 (93.3)	1843 (90.2)	0.18
- Statin	276 (92.3)	1917 (93.8)	0.39
- Beta blocker	247 (82.6)	1588 (77.7)	0.07
- Renin-angiotensin system blocker	208 (68.6)	1338 (65.5)	0.18

NSTEMI: non-ST-segment elevation myocardial infarction; PCI: percutaneous coronary intervention; STEMI: ST-segment elevation myocardial infarction; UA: unstable angina.

**Table 3: In-hospital events among young and older patients who underwent percutaneous coronary intervention.**

Events	Young patients (age ≤ 45 years old) N = 308 n (%)	Older patients (age ≤ 45 years old) N = 2118 n (%)	P-value*
Ventricular tachycardia	4 (1.3)	21 (1.0)	0.84
Heart failure	31 (10.1)	173 (8.2)	0.31
Cardiogenic shock	4 (1.3)	14 (0.7)	0.44
Acute renal failure	3 (0.97)	7 (0.3)	0.20
Emergency Coronary bypass surgery	0 (0)	3 (0.1)	0.63
Stent thrombosis	3 (0.97)	8 (0.38)	0.33
Major bleeding	4 (1.3)	20 (0.94)	0.77
Cardiac death	3 (0.97)	18 (0.85)	0.91

\*All p-values were non-significant for all events in multiple binary logistic regression.

**Table 4: Cardiovascular events at 1 and 12 months among young and older patients who underwent percutaneous coronary intervention.**

Events	Young patients (age ≤ 45 years old) N = 308 (%)	Older patients (age ≤ 45 years old) N = 2118 (%)	P-value*
From hospital admission to one month:			
- Cardiac death	1.63	1.28	0.81
- Stent thrombosis	1.30	1.44	0.95
- Major bleeding	1.30	1.08	0.96
- Readmission for:			
- Acute coronary syndrome	2.30	2.02	0.97
- Heart failure	0.99	0.58	0.65
- Target vessel or lesion revascularization	0.99	1.39	0.77
From hospital admission to 1 year:			
- Cardiac death	11 (3.63%)	44 (2.11%)	0.15
- Stent thrombosis	11 (3.63%)	43 (2.08%)	0.13
- Major bleeding	4 (1.30%)	25 (1.18%)	0.92
- Readmission for:			
- Acute coronary syndrome	19 (6.29%)	120 (5.82%)	0.84
- Heart failure	7 (2.32%)	28 (1.36%)	0.29
- Target vessel or lesion revascularization	11 (3.65%)	67 (3.24%)	0.84

\*All p-values were non-significant for all events in multiple binary logistic regression

## DISCUSSION

The main findings of this study are: about 13% of Middle Eastern patients admitted with ACS or stable coronary

disease who underwent PCI were < 45 years of age; the prevalence of major cardiovascular risk factors in young patients was similar to that in older patients, and the incidence rates of the major adverse cardiovascular

events at one year in the young patients were not different from those in the older age groups.

There is no uniform definition of “young” used in the published clinical studies and registries that evaluated cardiovascular risk profiles of young patients. Although 45 years of age or younger is the age used more often than others; studies defined age as <35 years, <40 years, <44, <46 years, <50, and <55 years.<sup>10-26</sup> Young patients, in general, account for <12% of CAD or ACS patients.<sup>21,27</sup> Studies reported percentages as low as 2.6% and 5.8%, and as high as 8% and 11.6%; less than the 13% reported in this study.<sup>10,13,21,27,28</sup> Moreover; the number of young patients included in this study (308 patients) is larger than that reported by other investigators which was as low as 43 and 81 patients, and as high as 195 patients.<sup>12,27,29</sup> The study that reported data of more than 2000 of young patients was a 7-year nationwide registry.<sup>14</sup>

There are an increasing number of young patients admitted with ACS or who undergo PCI. This is most likely due to the increasing prevalence of cardiovascular risk factors in younger age groups, including DM, dyslipidemia, cigarette smoking, metabolic syndrome, obesity, and illicit drug use.<sup>30,31</sup> The studies that compared prevalence of risk factors in young and older patients yielded inconsistent findings. Cigarette smoking is the most common risk factor in CAD in young patients with a prevalence that reaches up to 92%.<sup>32</sup> In countries where cigarette smoking is prevalent in all age groups, such as the Middle East, this risk factor is not expected to be higher in the young CAD patients compared with older patients. The incidence of DM in younger age groups is increasing, especially in the Middle East.<sup>31,33</sup> Individuals <44 years of age and women are experiencing the greatest increase in incidence of DM and obesity since the 1980s.<sup>34</sup> Additionally; the risk of MI associated with incident DM or metabolic syndrome is higher in younger women than any other group, increasing their odds of MI almost five-fold.<sup>35</sup> This study showed a prevalence of DM of 56% in young CAD patients, higher than the 20-30% prevalence reported by others.<sup>12,17,35</sup> Unlike the studies that showed lower prevalence of DM, hypertension, hypercholesterolemia and lower blood levels of high-density lipoprotein cholesterol in the young compared with older patients; this study did not show such differences, a finding we share with others.<sup>21,36</sup>

In addition to the classical cardiovascular risk factors; physical and psychological triggers and stresses can also play an important role in the incidence of CAD and ACS in young patients. These factors, however, are not routinely addressed during admission.<sup>35,37</sup> The use of illicit drug; cocaine in particular, was observed in 36% of young patients admitted with ACS in some western studies.<sup>11</sup> Although this habit is not prevalent at a large scale in Middle Eastern communities compared to the other regions; we did not subject the young patients to routine blood or urine drug screen tests.<sup>19,38,39</sup>

The clinical presentation of CAD in young patients differs from that in their older counterparts. The majority of young CAD patients present with ACS and only one-fourth present with stable coronary syndrome.<sup>38</sup> Furthermore; young patients have STEMI more than NSTEMI.<sup>15,21</sup> This study indicates that there was no difference in the prevalence of ACS or STEMI in the young and the older patients who underwent PCI. About half of the young patients in this study had single-vessel CAD, less than higher rates reaching up to 70% reported by others.<sup>12,21,38</sup> High prevalence of DM and other risk factors in young patients in present study may explain this finding.

Young patients, in general, have better prognosis in the earlier period after admission with MI than older patients due to low-risk profile, presence of single-vessel CAD, and utilizing aggressive diagnostic and revascularization strategies at higher rates compared with older patients when admitted with ACS.<sup>7,21,22, 28,37,38</sup>

Most of published studies of outcome in young patients limited their data to the in-hospital adverse events with a mortality rate that ranged between 1.6% and 3%.<sup>11,17</sup> These rates were not necessarily lower than those observed among older patients, as demonstrated by the current study, where the in-hospital mortality rates in the young and older patients were not different (0.97% and 0.85%; respectively). One year death rate in young patients in our study (3.6%) was not very different from those reported by other studies, and ranged between 1% and 4.8%.<sup>14,35,39</sup> In concordance with other investigators; we did not find a favorable outcome (death, revascularization, ST or major bleeding) in young compared with older patients.

Potential explanations of the absence of a better outcome in the young group include the absence of a favorable risk profiles and the presence of multivessel CAD in about half of the young age group. Furthermore, the survival gap at one year in the two age groups could have narrowed due to the fact that the whole study population underwent PCI, a procedure that is associated with an improved outcome especially in ACS patients with advanced age.

There is a significant socioeconomic impact of the increasing number of young patients admitted with CAD and ACS. These patients potentially have longer life expectancy than the elderly and thus may require further admissions for life-threatening cardiovascular events and revascularization procedures. Frequent hospital admissions and readmissions of young patients with ACS and the associated morbidity and mortality may also impact the nation's workforce as a whole, and the national health budget.<sup>7,18</sup> It is of vital importance to reevaluate the national strategies that address the primary and secondary cardiovascular prevention in younger age groups in order to control the cardiovascular epidemic in present region.

A few limitations in present study warrant discussion. Inherent to similar observational registries; the study is subject to selection bias, collection of non-randomized data, and missing or incomplete information. ACS patients who died before or shortly after admission and those who do not undergo angiography were not represented in this study. We included only patients who underwent PCI; hence, the conclusions may not apply to all ACS patients not treated by invasive approach.

## CONCLUSION

In conclusion, Middle Eastern young patients account for 13% of all patients undergoing PCI. Their clinical and coronary angiographic features are not different from those in older patients. One-year outcome in young patients is not better than that in the older patients.

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