Acute myocardial infarction among young adults under 40 years of age. Risk factors, clinical and angiographic characteristics

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SOUHRN

U mladých dospělých se zvláštními specifiky se ischemická choroba srdeční vyskytuje stále častěji; i když je považována za jednu patologickou jednotku, nejedná se o výjimečné případy.
Metody: Na kardiologickém oddělení B nemocnice ibn Sina Hospital v marockém Rabatu jsme v období od ledna 2011 do prosince 2018 provedli retrospektivní studii. Do studie byli zařazeni všichni pacienti přijatí s diagnózou infarktu myokardu, kteří byli ve věku 40 let nebo mladší. Statistická analýza se prováděla pomocí software SPSS.
Výsledky: Do studie bylo zařazeno celkem 80 pacientů, které jsme rozdělili do dvou skupin: skupiny 1 s obstrukční ischemickou chorobou srdeční (49 pacientů) a skupiny 2 s neobstrukční ischemickou chorobou srdeční (31 pacientů). Kuřáctví a užívání návykových látek statisticky významně převládaly u pacientů ve skupině 1 (73,5 % vs. 41,9 %; $p = 0,005$) oproti skupině 2 (53,1 % vs. 22,6 %; $p = 0,007$). Pacienti ve skupině 2 navíc měli méně často hypertenzi a dyslipidemii i prodromální symptomy (28,6 % vs. 6,5 %; $p = 0,01$; resp. 24,5 % vs. 3,2 %; $p = 0,01$; resp. 32,7 % vs. 12,9 %; $p = 0,047$); nepřítomnost faktorů rizika srdečních onemocnění byla ve skupině 2 významná ($p < 0,001$). Ve skupině 1 převládalo postižení jedné tepny (43,5 %), přičemž ve skupině 2 prokázalo angiografické vyšetření svalový můstek (1,25 %), aneurysma koronární tepny (1,25 %), vazospasmus (2,5 %), nevýznamné léze (13,75 %) a nepostižené tepny (20 %).
Závěr: Základem léčby je i nadále ovlivňování hlavních rizikových faktorů, zvláště kuřáctví a užívání návykových látek u mladé marocké populace. Vzhledem k různé etiologii postižení u této mladé populace je nutno při klasické léčbě zaměřit pozornost i na etiologický aspekt.

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ABSTRACT

Coronary artery disease is becoming more frequent in young adults with specificities of its own. It is considered as a singular entity, and yet not exceptional one.
Methods: We conducted a retrospective study in the Cardiology Depratment B of ibn Sina Hospital in Morocco, Rabat between January 2011 and December 2018. The study included all patients admitted with a diagnosis of myocardial infarction and whose age was equal or less than 40 years. The statistical analysis was performed using SPSS Software.
Results: In the study period, 80 patients were included. We separated patients in 2 groups: group I with obstructive coronary artery disease (49 patients) and group II with nonobstructive coronary artery disease (31 patients). Smoking and substance abuse were significantly predominant in patients of group I with respectively (73.5% vs 41.9%; $p = 0.005$; 53.1% vs 22.6%; $p = 0.007$). Moreover, patients of group II had less hypertension and dyslipidaemia and prodromal symptoms (28.6% vs 6.5%; $p = 0.01$; 24.5% vs 3.2%; $p = 0.01$; 32.7% vs 12.9%, $p = 0.047$) and the absence of cardiac risk factors in group II was significant ($p < 0.001$). Single-vessel involvement was predominant (43.5%) in group I and angiographic findings in group II showed: myocardial bridge (1.25%), coronary aneurysm (1.25%), vasospasm (2.5%), non-significant lesions (13.75%) and normal arteries in 20%.
Conclusion: The prevention of risk factors remains the cornerstone of the treatment, especially smoking and drug use among young Moroccan population. The multiple aetiologies found in this young population induce an aetiology-targeted management along with the conventional treatment.

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Introduction

Despite all the advances in the diagnosis and management in medical fields; coronary artery disease (CAD) remains a leading cause of death worldwide.[1] The morbidity and mortality from acute myocardial infarction (AMI) declined over the last decades in the industrialised world, whereas they seem to have been progressively increasing in many developing countries.[2] Although CAD is considered as a disease occurring in older adults, young subjects can be affected. The devastating consequences of AMI in such active young adults are of a huge psychological impact, but also on the economic development as it leads to early retirement and reduces the ability to work. All these implications affect not only the patient but the family members too, and must be taken into consideration by the treating physicians.

AMI among young adults constitutes a particular and uncommon entity with its prevalence (less than 10%),[3] physiopathology and cardiac risk factor profiles. Most studies have used an age cut-off of less than or equal to 40 years to define young.[1,2,4]

The atherosclerosis process begins in the early stages of life but remains asymptomatic.[1] However, the trend for the increased prevalence of risk factors of CAD like smoking, hypertension and the preference for high-fat dietary habits is causing an advanced atherothrombotic state in young patients.[5] Studies showed that CAD in young subjects is usually limited to a single vessel with less extensive and severe lesions.[5] Young adults have a higher incidence of myocardial infarction with non-obstructive coronary artery than old patients.[6] Thus, the causes of AMI can be divided into two groups: obstructive CAD and nonobstructive CAD.

In this paper, we focused our attention on risk factors and clinical characteristics of a population of young adults in a developing country in North Africa such as Morocco according to their angiographic profiles.

Methods

We performed a retrospective analysis of all patients presenting to the Department of Cardiology B in Rabat, Morocco, between January 2011 and December 2018. We enrolled in this study 80 young adults with AMI and aged less than or equal to 40 years. The diagnosis of myocardial infarction was based on the presence of evidence of AMI including elevated cardiac biomarkers (troponin: with a value above the 99th centile upper reference limit [14 ng/L]) and symptoms of ischemia or electrocardiogram changes suggesting new ischemia in two or more contiguous leads or new left bundle branch block. Exclusion criteria are patients age younger than 18 years or older than 40 years, patients with pre-existing heart failure, valvular or pericardial diseases, patients diagnosed with myocarditis or tako-tsubo.

We collected baseline patient's data: Epidemiological details like age and gender, medical history, clinical and electrocardiogram characteristics at presentation. Physical examination at admission was recorded. Traditional cardiac risk factors for CAD were also noted including smoking status (patients currently smoking or stopped less than a year were considered smokers and others were non-smokers). The consumption of cocaine, marijuana, and alcohol was recorded.

Left ventricular ejection fraction (LVEF), angiographic findings and therapeutic management were investigated and reported.

Obstructive coronary disease was defined as at least a 70% narrowing in the diameter of the left anterior descending or the left circumflex or the right coronary arteries, or $\geq$ 50% reduction in the left main artery. The number and the type of diseased vessels which were involved were noted and obstructive CAD was classified as one or two or three vessels disease. Patients with normal, or coronary spasm, or coronary aneurysm or minimal CAD were classified as having nonobstructive CAD. All patients with normal coronary arteries underwent cardiac magnetic resonance (MRI). Only patients with ischemia evidence in the MRI were included.

Concerning statistical analysis, all data were checked and analysed using SPSS software for Windows version 18 (SPSS. Inc. Chicago; Illinois). Continuous variables were expressed as mean and standard deviation. Comparison of categorical variables between groups was performed using chi-square or Fisher's exact test, p-value $\leq$ 0.05 was considered statistically significant.

Results

Over the study period; 1352 patients were admitted to our cardiac catheterization laboratory presenting AMI. Of these; 80 patients met the study criteria (5.9%). For the purpose of analysis and comparison, we distinguished two groups of patients on the grounds of their angiographic profiles: group I (n = 49) with obstructive CAD and group II (n = 31) gathered patients with nonobstructive CAD. Epidemiological, risk factors and clinical characteristics according to their angiographic findings are shown in Table 1. The mean age of our 80 patients was 35.3 (± 4.6) years with a minimum of 21 years a maximum of 40 years old. Among these patients 73.8% were males and 26.3% were females. Smoking 61.3% was the most frequent risk factor recorded, and less frequently: hypertension 20%, dyslipidaemia 16.3%, and family history of CAD in 13.8%. We found that 18.8% patients didn't present any of the studied risk factors. The group with obstructive CAD (group I) had a higher proportion of male patients compared to the group having nonobstructive CAD (group II) but with no difference statistically significant. Cardiac risk factors like: Hypertension, dyslipidaemia, smoking and substance consumption were more frequently observed in group I than group II with respectively (28.6% vs 6.5%; p = 0.01; 24.5% vs 3.2%; p = 0.01; 73.5% vs 41.9%; p = 0.005; 53.1% vs 22.6%; p = 0.007). The group without obstructive CAD had 38.7% of patients without any of the studied atherosclerosis risk factors versus 6.1% of group I; p < 0.001.

One male patient had a history of Behcet's disease and three female patients had a history of Takayasu disease.

Of all the patients with obstructive-CAD, 16 had warning symptoms for at least 3 weeks before admission such

as chest pain history and only 4 patients from group with nonobstructive CAD which reached the statistically significance level, *p* = 0.047.

The most common symptom at admission was typical chest pain which was present in 75% of all 80 patients.

As shown in Table 2; ST segment elevation myocardial infraction (STEMI) was more frequent than non-ST segment elevation myocardial infraction in both groups. In echocardiography, the group with obstructive CAD had a significantly higher number of patients with wall mo-

tion abnormalities at admission. However, group I had a lower LVEF than group II without any significant difference.

The single vessel involvement was the main angiographic pattern in our study among patients with obstructive CAD; as summarized in Table 3; with 43.7%, followed by two-vessels disease in 12.5% and three-vessels disease in 5%. The significant coronary lesions mainly affected the left anterior descending (LAD) artery in 43.7%. only 2 patients had the left main coronary artery involved, in

Table 1 – Demographic and clinical findings

	Obstructive-CAD Group I (n = 49)	Nonobstructive CAD Group II (n = 31)	*p*-value
Age (years)	35.8 (± 4.4)	34.4 (± 4.9)	NS
Male gender, n (%)	38 (77.6)	21 (67.7)	NS
Hypertension, n (%)	14 (28.6)	2 (6.5)	0.01
Diabetes, n (%)	8 (16.3)	1 (3.2)	NS
Dyslipidaemia, n (%)	12 (24.5)	1 (3.2)	0.01
Type of dyslipidemia, n (%) Hypo-HDL Hyper-TG Hyper-LDL	10 (20.4) 1 (2) 1 (2)	0 (0) 1 (3.2) 0 (0)	NS
Substance use, n (%)	26 (53.1)	7 (22.6)	0.007
Type of substance used, n (%) Marijuana Cocaine Alcohol Marijuana + alcohol	12 (24.5) 2 (4.1) 6 (12.2) 6 (12.2)	3 (9.7) 0 (0) 0 (0) 4 (12.9)	0.03
Smoking, n (%)	36 (73.5)	13 (41.9)	0.005
Smoking quantity, n (%) ≤ than 20 cigarettes/day ≥ than 20 cigarettes/day	11 (22.4) 25 (51)	4 (12.9) 9 (29)	0.001
Obesity, n (%)	14 (28.6)	6 (19.4)	NS
Family history of CAD, n (%)	5 (10.2)	4 (12.9)	NS
Without crdiac risk factor, n (%)	03 (6.1)	12 (38.7)	< 0.001
History of chest pain, n (%)	16 (32.7)	4 (12.9)	0.047
Takayasu arteritis, n (%)	1 (2)	2 (6.5)	NS
Behcet's disease, n (%)	0 (0)	1 (3.2)	NS
History of stroke, n (%)	1 (2)	2 (6.5)	NS
Typical chest pain, n (%)	38 (77.6)	22 (71)	NS
Dyspnea, n (%)	6 (12.5)	6 (19.4)	NS
Sweating, n (%)	23 (46.9)	21 (67.7)	NS
Palpitation, n (%)	8 (16.3)	0 (0)	0.02

Table 2 – Electrical and echocardiographic findings

	Obstructive CAD Group I (n = 49)	Nonobstructive-CAD Group II (n = 31)	*p*-value
STEMI, n (%)	36 (73.5)	20 (64.5)	NS
Left bundle block, n (%)	3 (6.1)	2 (6.5)	NS
Q waves, n (%)	7 (14.3)	7 (22.6)	NS
Normal chest X-ray, n (%)	44 (89.8)	26 (83.9)	NS
Wall-motion abnormalities, n (%)	44 (89.8)	21 (67.7)	0.01
LVEF, mean (± SD)	48.1 (± 12.9)	54.1 (± 13.2)	NS

Table 3 – Coronary angiographic findings in Group I and Group II			
Angiographic features in Group I	**n (%)**	**Angiographic features in Group II**	**n (%)**
Number of vessels with stenosis, n (%) 1-vessel 2-vessel 3-vessel	35 (43.7) 10 (12.5) 4 (5)	Coronary artery aneurysm	1 (1.25)
The involved vessel, n (%) LAD LCX RCA Left main coronary artery	35 (43.7) 8 (10) 11 (13.7) 2 (2.5)	Coronary spasm	2 (2.5)
		Non-significant CAD	11 (13.75)
		Myocardial bridge	1 (1.25)
		Normal coronary arteries	16 (20)

Table 4 – Therapeutic management and readmission within 2 years after discharge			
	Obstructive-CAD Group I (n = 49)	**Nonobstructive-CAD Group II (n = 31)**	***p*-value**
Revascularization	32 (65.3%)	4 (12.9%)	**< 0.001**
Thrombolysis	9 (18.4)	4 (12.9%)	NS
Successful thrombolysis	2 (4.1%)	4 (12.9%)	**0.02**
Percutaneous coronary intervention	29 (59.2%)	0 (0%)	**< 0.001**
Coronary artery bypass graft	3 (6.1%)	0 (0%)	NS
Readmission	10 (20.4%)	0 (0%)	**0.007**

both cases they were associated with LAD lesions. One of these patients with left main coronary artery involvement had a history of Takayasu disease.

Among group I; a 30-year-female patient with no conventional risk factor had a simultaneous thrombosis of the LAD and the circumflex artery. The etiological diagnosis showed an anti-thrombin III deficiency. Another female patient in group I was diagnosed with familial hypercholesterolemia.

In group II; with nonobstructive CAD; multiple underlying mechanisms were noted in Table 3. One patient with coronary artery aneurysm in the proximal segment of LAD had a history of Behcet's disease. Two patients showing spastic occlusion on the LAD had both asthmas in their medical history; and one of these patients was diagnosed with Churg-Strauss syndrome.

During hospitalization, percutaneous coronary intervention (PCI) and coronary artery bypass graft surgery (CABG) of the infarct-related lesions were performed in 29 (59.2%) and 3 (6.1%) patients respectively (Table 4). The others were put on medical conventional therapy. Long-term anticoagulation was indicated for 2 patients (Behcet's disease and anti-thrombin III deficiency). The patient presenting cardiac involvement in Churg-Strauss syndrome received a combination therapy of glucocorticoids and cyclophosphamide along with vasodilators. No patient needed the use of positive inotropic drugs.

Among patients presenting STEMI, thrombolysis was used in group I in 9 (18.4%) versus 4 (12.9%) patients in group II. Thrombolysis success criteria were observed in 12.9% of group with nonobstructive CAD compared to 4.1% of patients of group with obstructive CAD ($p = 0.02$).

There was no complication during hospitalisation and in-hospital mortality didn't record any death among our patients. Ten patients of group I were readmitted in our hospital within two years after their discharge. Six patients were readmitted for in-stent restenosis; previously received PCI on the LAD, one patient previously refused CABG and was readmitted for recurrent chest pain and the three others for new significant stenosis on other vessels.

Discussion

Even though ischemic heart disease is considered a disease of the older population[7] premature CAD remains a significant cause of morbidity and mortality in the world.[8] AMI in the young individuals represent a small but yet an important group to study its specificities in the era of preventive cardiology.

As expected, the male predominance found in our study has been previously reported and can be attributed to the protective effects of oestrogens against CAD.[9–11] The less incidence in young female can be also due to relative absence of smoking and substance abuse among Moroccan female, due to cultural reasons in the Arabian world. As it has been shown in our study, smoking appears to be the most common and important risk factor in both studied groups contributing to early atherosclerosis and AMI, which is consistent with international literature.[12,13] Cigarette smoking has a role in atherosclerosis process but also in non-atherosclerotic causes like increasing coronary vasospasm as well as thrombogenesis.[14] The pathophysiological mechanisms linking smoking and ischemic

heart disease have been widely reported as: endothelial dysfunction, inducing platelet aggregability and activation and blood viscosity.[15,16] These findings may explain the high frequency of nonobstructive CAD among young smokers. Hypertension and dyslipidaemia were more common in obstructive CAD than in nonobstructive patients, who were also more likely to be obese. The prevalence of obesity in our study was 28.6% versus 19.4%, similar findings were observed by other authors.[17,18] Genetic factors (family history of premature CAD and obesity) along with environmental ones may play an important role in this complex pathogenesis of CAD in young adults.[7]

Outside of conventional risk factors, substance use was significantly associated with obstructive CAD. Marijuana (cannabis) consumption was the most reported illicit drug in our study, especially in the group of patients having obstructive CAD. Due to previous strong evidences showing that marijuana and cocaine are risk factors and a trigger for AMI,[19,20] American guidelines have recommended; mostly in young patients < 50 years of age with AMI; a toxicology screening to be considered when we suspect substance abuse.[21]

Multiple and well-described effects of cannabis have been demonstrated linking it to the development of CAD through endothelial damage and increasing platelet aggregation. This substance leads also to plaque disruption and vasospasm explaining the normal or apparently normal coronary arteries in some young myocardial infarction cases.[20,22]

Cocaine seems to be involved in accelerating atherosclerosis process and coronary vasoconstriction either in stenotic or non-stenotic segment.[19] Cocaine users in our study had angiographically non-significant lesions, Defilippis et al. reported that there is a potential multi-substance effect in simultaneous consumption of substances like alcohol and opioids,[21] which was the case in both patients.

Patients in both groups complained mostly of typical chest pain, but the group with obstructive CAD experienced prodromal symptoms in 32.7%. These results suggest that this group had a preconditioning status caused by the premature atherosclerosis and then suffered from sudden interruption of coronary blood flow after plaque rupture. However, patients in this group (group I) tend to have less extensive and severe atheromatous lesions and frequently contained in one vessel (43.7%). These observations can be explained by the rapid progression of atherothrombosis more likely than a gradually evolving atherosclerosis.

Among the group with obstructive CAD (group I), two patients had a history of Takayasu. We believe that prothrombotic and inflammatory indices have contributed to the initiation and development of premature atherosclerotic lesions.[23]

Myocardial infarction with nonobstructive coronary arteries is an important subgroup; especially in young adults; representing 6% of all AMI cases.[24] Although, they represented smaller group compared to obstructive CAD group (49 vs 31) same finding was reported in Raparelli et al. study.[25] Our study established similar results to what have been previously observed in the literature such as: Less traditional risk factors, higher ejection fraction and

better prognosis than the obstructive group.[24,26,27] Specific testing to identify the underlying aetiology is crucial for aetiology-targeted management like: thrombophilia testing, provocative testing for vasospasm and intravascular ultrasound (IVUS). Through literature, the main potential mechanisms suggested in nonobstructive-CAD entity include: coronary spasm, coronary microvascular dysfunction, plaque disruption, spontaneous coronary thrombosis/emboli and coronary dissection.[28] In our study, 33.7% had normal arteries or non-significant lesions in coronary angiography, but since the angiography is usually performed later after admission in our centre (a delay of 1–5 days) and IVUS was not available, spontaneous thrombolysis or atherosclerosis with positive remodelling of the artery may be suggested.

Study limitations

Our research was limited to a large academic single center; the results may not be completely generalizable to other regions. This was a retrospective observational study over the past 8 years, and this long-time span includes variability like disease definitions and laboratory normal values. No follow-up data were presented since our study was based on in-hospital records only.

Conclusion

The current study showed a significant difference in cardiac risk factors and angiographic features in young Moroccan population. Smoking and substance use were the most important factors standing out and clearly involved in the myocardial infarction in young people in such a developing country. The need is to focus our efforts for an intense and aggressive primary prevention and to increase an awareness of the dangerous effects of cigarette and drug abuse.

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