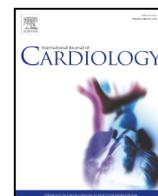




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Acute coronary syndrome among patients with chest pain: Prevalence, incidence and risk factors☆

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ABSTRACT

Background: Urbanization and adoption of new diet and lifestyles had increased the cardiovascular risk factor (CVRF) rate and therefore, acute coronary syndrome (ACS) in developing countries such as Tunisia. We aimed at determining ACS prevalence among a sample of Tunisian patients with chest pain, at establishing the standardized incidence rate (SIR) of ACS, and at quantifying the relationship between ACS and CVRF in this population. **Methods:** We studied 3158 patients admitted to a chest pain unit for non-traumatic chest pain collected in Emergency Data from January 2012 to December 2014. For all patients, the data were collected using a standardized form. We performed univariate rather than multivariate logistic regression analyses to identify age and gender-related CVRF in ACS. Linear interpolation was used for curve estimation. **Results:** 707 (22.3%) chest pain patients were classified as ACS. The age-SIR per 10^{-5} person year (PY) was 85.7; it was 112.6 in men and 45.3 in women. Eighty one percent of patient with ACS cumulated 2 CVRF and more. The highest odds ratio were 2.00 (95% CI 1.64–2.44) for diabetes and 1.81 (95% CI 1.50–2.18) for active smoking. ACS in elderly patients was significantly associated with active smoking (OR: 2.36), diabetes (OR: 1.72) and personal ACS history (OR: 1.71). We found a significant and very high linear relation between the number of CVRF and ACS odds ratio ($R^2 = 0.958$). **Conclusion:** Our results showed that the incidence of ACS in a Tunisian population is not very different from what is observed in developed countries; with a close relation with CVRF especially diabetes and smoking.

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1. Introduction

Ischemic heart disease is a world public health problem. In USA, there are more than 2 million people hospitalized each year for chest pain suggestive of acute coronary syndrome (ACS) [1]. In Tunisia, one of the Eastern Mediterranean Region (EMR), cardiovascular diseases (CVDs) causes 49% of death [2] and 19.3% of the number of years of life lost [3]. Seventeen percent of CVD mortality were related to coronary heart disease (CHD) [4]. Although, olive oil consumption is

very common [5], the frequency of CVRF among coronary patients in Tunisia tends to be comparable to developed countries [6]. However, true incidence of acute coronary syndrome (ACS) is still unknown and weakly documented. Several multinational registries of ischemic heart disease included Tunisia in their statistics such as TEPS-ACS 2009, ACCESS and European Heart Survey but selected only patients with ACS without giving objective data about the actual incidence or prevalence of this syndrome in the country.

The aim of our study was to determine the prevalence of ACS among a cohort of chest pain patients in the Emergency Department (ED), to establish the incidence rate of ACS in Monastir city, and to quantify CVRF burden in ACS patients.

2. Methods

2.1. Design

This is a prospective study performed in public structures that drain all the cases with suspected SCA.

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2.2. Study population

Patients were included in our study regardless to their age, gender or origin, once admitted to Monastir District at University Hospital Emergency for non-traumatic chest pain from January 2012 to December 2014. Deaths from ACS at home were not included. All patients with non-traumatic chest pain and suspected to have SCA in Monastir governorate, were explored in the university hospital ED which contains two interventional cardiology services. The ACS was defined according to current European guidelines [7]: electrocardiographic changes consistent with ACS, serial increases in cardiac biomarkers of necrosis, or documented coronary artery disease. Patients were diagnosed with ST(–) segment elevation myocardial infarction (STEMI), non-STEMI (NSTEMI), or unstable angina pectoris using standardized criteria. We have considered the control population, patients with non-traumatic chest pain and who have had other disease (not SCA).

For all patients (SCA and not SCA), the data were collected using a standardized form including demographic characteristics, and clinical examination data counting cardiovascular risk factors and coronary disease history.

The socio-demographic variables recorded were age, sex, and professional status (the following categories were used: manual workers in industry, assistant non-manual employees, professionals with occupations requiring normally ≥ 3 years of university or college education; others: housewives, non-professional self-employed, military, and others). Age-adjusted to sex is defined by age more than 55 years for men and more than 65 years for women. Current smokers were defined as those who smoked at least one cigarette per day. In all participants a detailed medical history was recorded, including family history of CVD as well as personal history of hypertension, hypercholesterolemia, hypertriglyceridemia and diabetes. Patients whose average blood pressure levels were $\geq 140/90$ mm Hg or were under antihypertensive medication were classified as having hypertension. Dyslipidemia was defined as total serum cholesterol levels >200 mg/dL or the use of lipid-lowering agents; and diabetes mellitus was defined as fasting blood glucose >126 mg/dL or the use of anti-diabetic medication. The number of CVRF was calculated by their sum.

Data were analyzed using descriptive, uni-variate and multivariate statistical analysis. Statistical Package for Social Science (SPSS) software version 18.0 was used to analyze the data. The crude incidence rate of ACS was calculated based on the Tunisian INS population [8]. The age-standardized incidence rate per one million person-years (PY) was calculated among the world standard population according to WHO statement 2013 [9]. Non-normally distributed continuous variables (age) was presented as median value [min–max]. Categorical variables (sex, smoking habits, medical history, socioeconomic status, CVD risk factors) were presented as a proportion and compared with χ^2 -test to identify significant determinants. p-Values of <0.05 were considered significant. Risk factors, related to ACS with $p < 0.20$ criteria were included in multivariate logistic regression models, and the results were expressed as odds ratios with 95% confidence intervals (CI). Linear interpolation was used for curve estimation.

3. Results

Among patient with non-traumatic chest pain ($n = 3158$), 707 were classified as ACS (22.3% [95% CI 20.9–23.7]) (Table 1). We estimated 5021 the number of cases in Tunisia in 2014. In a period of three

Table 1
Cause of chest pain ($n = 3158$).

Extracardiac n (%)	2428 (76.9)
Parietal pain n (%)	1568 (49.7)
Pleuropulmonary	151 (4.8)
Cardiac n (%)	730 (23.1)
Acute coronary syndrome	707 (22.3)

years, the number of cases increased from 220 in 2012 to 250 in 2014 ($p = 0.863$) and from 41 to 43/10⁵ H in crude incidence rate (CIR). Incidence rates were higher among the population aged over 60 years (259/10⁵ H) ($p < 10^{-4}$) and among men compared to women ($p = 0.003$). The age-standardized incidence rate was 85.7/10⁵ PY with 112.6/10⁵ PY in men and 45.3/10⁵ PY in women (Table 2).

HTA, diabetes and dyslipidemia are more frequent in women presenting ACS than Men. Whereas active smoking proportions were more frequent in men and patient aged less than 65 years. Eighty one percent of patient with ACS cumulated 2 risk factors and more (Table 3). The odds ratio was 2.00 (95% CI 1.64–2.44) for diabetes, 1.81 (95% CI 1.50–2.18) for active smoking. Women had the highest risk for dyslipidemia 1.78 (95% CI 1.3–2.5). ACS in elderly patients was significantly associated with active smoking (OR: 2.36), diabetes (OR: 1.72) and coronary artery disease history (OR: 1.71). The OR was 2.51 (95% CI 1.63–3.87) for patients with only one risk factor and 10.56 (95% CI 6.80–16.38) for those who had cumulated four risks (Table 4). Correlation and linear regression analyses showed a significant and very high linear relationship between the number of risk factors and ACS odds ratio: $R^2 = 0.958$ for the overall group and $R^2 = 0.992$ for patients aged less than 65 years; $R^2 = 0.474$ in elderly patients (Fig. 1).

4. Discussion

We have determined the prevalence of ACS among a sample of Tunisian patients with chest pain from a university emergency department. It was 22.3%, and the age-SIR per 10⁵ was 112.6 for men and 45.3 for women. Likewise we have quantified the cardiovascular risk factors in ACS population, and identified a very high linear relation between cumulative risk factors and ACS.

Today, following the demographic and epidemiological transition experienced by our country, cardiovascular diseases represent a major public health problem and the leading cause of death in Tunisia by an overall mortality rate of 49% in 2014 [4]. But studies that were focused in the incidence of ACS in developing countries are rare and not updated. In addition, it is inappropriate to extrapolate systematically data derived from surveys conducted in developed regions [10–15]. In Tunisia, the latest epidemiological survey is dated back to 2009 including five Tunisian hospitals. It was a project conducted in collaboration with European academic institutions: Newcastle University (UK),

Table 2
Crude and standardized incidence rates of ACS in Monastir (Tunisia).

	Cases	p	CIR/10 ⁵ H	Age-SIR/10 ⁵ H
Year				
2012–2014	707		43	
2012	220	0.863	41	
2013	235		43	
2014	252		46	
Age (2012–2014) years				85.7
<40	26	<10⁻⁶	5	
40–60	290		98	
>60	391		259	
Sex (2012–2014)				
Men	469	0.003	59	112.6
Women	238		31	45.3

ACS: acute coronary syndrome; CIR: crude incidence rate; SIR: standardized incidence rate.

707: Among 3,158 patients admitted at university hospital emergency for non traumatic chest pain from January 2012 to December 2014, 707 had have acute coronary syndrome. **0.863**: We have recorded an increase in the number of cases from 2012 to 2014 without significance. **–6**: the number of cases with SCA was statistically higher in elderly patients (>60 years). **43**: the crude annual incidence (calculated based on the Tunisian INS population). **85.7**: The age-standardized incidence rate: age adjustment of ACS incidence (calculated among the World standard population according to WHO statement 2013). **112.6**: The age-standardized incidence rate per men (calculated among the World standard population according to WHO statement 2013). **45.3**: The age-standardized incidence rate per women (calculated among the World standard population according to WHO statement 2013).

Table 3
Distribution of conventional cardiovascular risk factors by age and sex.

	All	N (%)			
		Men	Women	<65 years	≥65 years
Cardiovascular risk factors					
Age adjusted with sexe	422 (59.7)				
HTA	401 (56.7)	224 (47.8)	177 (74.4)*	223 (49.6)	178 (69.3)*
Diabetes	354 (50.1)	202 (43.1)	152 (63.9)*	216 (48.0)	138 (53.7)
Active smoking	299 (42.3)	292 (62.3)	7 (2.9)*	211 (46.9)	88 (34.2)**
Dyslipidemia	281 (39.7)	157 (33.5)	124 (52.1)*	168 (37.3)	113 (44.0)
Coronary family history	135 (19.1)	92 (19.6)	43 (18.1)	96 (21.3)	39 (15.2)***
Coronary personal history	212 (30)	149 (31.8)	63 (26.5)	120 (26.7)	92 (35.8)***
Number of Cardiovascular risk factors					
0	28 (4.0)	14 (3.0)	14 (5.9)	28 (6.2)	0 (0.0)
1	108 (15.3)	71 (15.1)	37 (15.5)	93 (20.7)	15 (5.8)
2	191 (27.0)	137 (29.2)	54 (22.7)	129 (28.7)	62 (24.1)
3	183 (25.9)	104 (22.2)	79 (33.2)	107 (23.8)	76 (29.6)
4	135 (19.1)	91 (19.4)	44 (18.5)	59 (13.1)	76 (29.6)
=5	62 (8.8)	52 (11.1)	10 (4.2)*	34 (7.6)	28 (10.9)*

*p value < 10⁻³; **p value < 0.005; ***p value < 0.05.

Liverpool University (UK) and Trinity College Dublin (Ireland) including four Mediterranean countries (Palestine, Syria, Tunisia and Turkey) with the main aim was to assess outcome of CHD. The results showed that mortality rates age adjusted of CHD rose by 20% in Tunisia and by 65% in Syria, and fell by 12% in Palestine and 17% in Turkey [12]. Our study assessed the prevalence of ACS among subjects with chest pain and found that it was lower than that described in Spain (29.5% in 2007) [16] and Italy (25% in 2011) [17]. We have notified 707 new ACS during three years, and we estimated to 5021 the number of cases in Tunisia during 2014. In USA, 620,000 subjects per year had a new coronary attack and 295,000 have a recurrent attack [7].

In our study, the age-SIR per 100,000 was 112.6 for men which is lower than the rates described in England (154/10⁵ in 2010), in Scotland (255/10⁵ in 2009) and in France (250/10⁵ in 2008) [18]. It was 45.3 for women in our study, higher than the rate described in England (34/10⁵), lower than described in Scotland (113/10⁵) and similar to the French SIR (50/10⁵) [18]. The sex-difference has been widely described in the literature [19]. Pelletier and all related it to the sex-related differences in access to care among patients with ACS [20]. Our study found that crude incidence rates of ACS increases with age and reaches 259 cases per 100,000 population aged more than 60 years. The incidence of ACS in Young patients is equivalent with literature

Table 4
Odds ratio of cardiovascular risk factors for developing ACS by gender and age, according to multivariate analysis.

	All	OR-95% CI			
		Men	Women	<65 years	≥65 years
Cardiovascular risk factors					
Age adjusted with sexe	1.68 [1.41–2.03]*				
HTA	1.24 [1.01–1.52]**	1.54 [1.2–2.0]*	1.46 [1.1–2.1]**	1.59 [1.3–2.0]*	0.89 [0.6–1.3]
Diabetes	2.00 [1.60–2.38]*	1.86 [1.4–2.4]*	2.20 [1.6–3.1]*	2.11 [1.6–2.7]*	1.72 [1.2–2.4]*
Active smoking	1.81 [1.50–2.18]*	1.51 [1.2–1.9]*	1.03 [0.4–2.5]	1.78 [1.4–2.2]*	2.36 [1.7–3.3]*
Dyslipidemia	1.24 [1.01–1.48]**	0.98 [0.7–1.3]	1.78 [1.3–2.5]*	1.24 [0.9–1.6]	1.26 [0.9–1.8]
Coronary family history	1.13 [0.90–1.43]	1.22 [0.9–1.6]	0.92 [0.6–1.4]	1.15 [0.9–1.5]	1.07 [0.7–1.7]
Coronary personal history	1.80 [1.44–2.25]*	1.88 [1.4–2.5]*	2.24 [1.5–3.3]*	2.00 [1.5–2.7]*	1.71 [1.2–2.4]*
Number of cardiovascular risk factors					
0	1	1	1	1	1
1	2.51 [1.63–3.87]*	2.25 [1.2–4.1]***	2.61 [1.4–4.9]***	2.45 [1.6–3.8]*	1.44 [0.8–2.7]
2	5.00 [3.30–7.57]*	5.50 [3.1–9.8]*	3.62 [2.0–6.7]*	5.43 [3.5–8.3]*	2.28 [1.2–4.2]***
3	7.52 [4.94–11.45]*	6.75 [3.7–12.2]*	8.04 [4.4–14.6]*	8.13 [5.2–12.7]*	3.70 [2.0–6.9]*
4	10.56 [6.80–16.38]*	11.38 [6.2–20.9]*	8.40 [4.4–16.0]*	10.0 [6.1–16.5]*	2.91 [1.4–6.0]***
=5	10.51 [6.39–17.30]*	9.36 [4.9–17.9]*	9.36 [3.7–23.7]*	12.74 [7.1–23.1]*	

ACS: acute coronary syndrome; *p value < 10⁻³; **p value < 0.05; ***p value < 0.005.

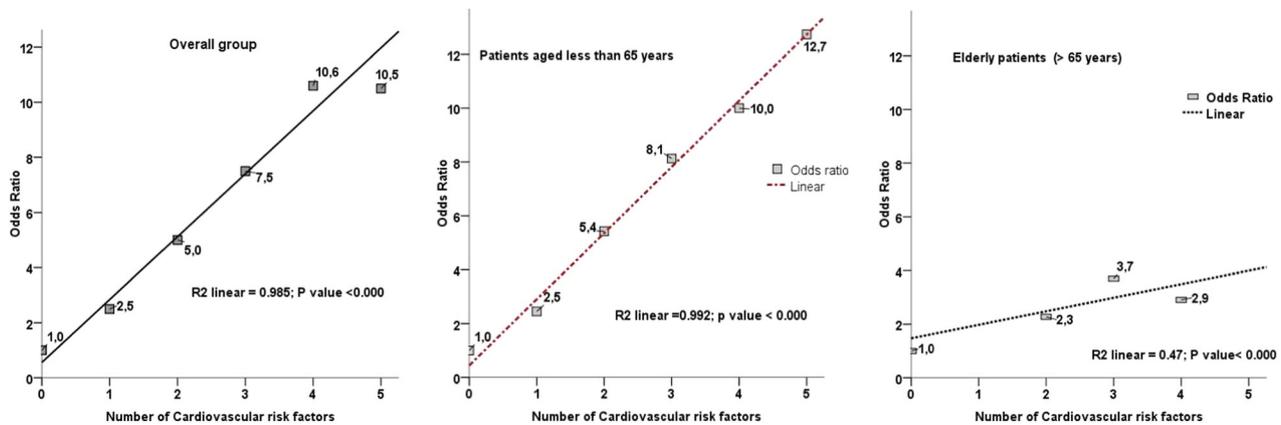


Fig. 1. Curve estimation of linear regression for predicting odds ratio through number of cardiovascular risk factors.

[21]. Lower in-hospital mortality rate and with shorter length of stay [21,22]. In Spain, the incidence of ACS underwent a remarkable decrease (21%) from 2002 to 2011 after the introduction of smoking restriction laws in public places [18]. Likewise, according to the Register of Latvia, there was a significant decrease in the incidence of ACS between 2005 and 2010 (82% in 2005 to 75% in 2010 for NSTEMI, and 18% in 2005 to 25% in 2010 for STEMI) [23].

In our study, 96% of patients with CHD have conventional risk factors more than those described in USA in 2003 (80% to 90%) [24]. The conventional risk factors in ACS patients described in our survey were those described in literature [25–28]. Diabetes and HTA are more frequent in our ACS population than that described in USA in 2003 [24].

The first limitation to our study is related to selection bias because the study involved only patients seen in public emergency departments. Other ACS cases have not been considered such as silent myocardial infarction and other ACS patients admitted elsewhere. According to our population behavior, the proportion of these patients is not significant. The second limitation is related to a misclassification of patient diagnosis. Although ACS in our study was defined on the basis of clinical, electrocardiographic and biomarkers we cannot rule out some diagnostic errors. It is thus possible that a limited number of patients were incorrectly classified as having or not ACS. In this study we have included in comparison to patients with SCA only non-traumatic chest pain patients who could have had some differences from the general population.

Conflict of interest

The authors have nothing to disclose concerning this manuscript.

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Ethical statement

The study was conducted under Good Clinical Practice conditions and according to the ethical standards.

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