Short and Long Term Outcomes of Patients Presenting with Acute Coronary Syndrome without ST Segment Elevation (NSTE-ACS): Findings from a Tunisian Register: The ReSCUS Register

Yaakoubi H*, Youssef R, Boukadida L, Jaballah R, Ben Salah H, Zorgati A and Boukef R

Department of Emergency, Chu Sahloul Sousse, Tunisia

Abstract

Background: Chest pain is one of the most common complaints in the emergency department. Acute coronary syndrome with ST segment elevation remains the ultimate medical emergency. However, acute coronary syndrome without ST segment elevation (NSTE-ACS) has an equivalent prognosis risk. The major challenge of the emergency physician is the rapid and accurate identification of patients with ACS who would benefit from immediate care.

Objective: Evaluation of our practices according to European Recommendations for management of NSTE-ACS and assessment of short and long term prognosis for Major Cardiovascular Events (MACE).

Methods: This is an analytical study, involving 850 patients treated for NSTE-ACS during a period of 2 years in our emergency department. The data was collected from our local register for acute coronary syndrome: ReSCUS register. The main results were: the different delays for medical care, length of stay in the emergency department, short-term complications and the occurrence of MACE registered at one month, six months, and one year later.

Results: The average age of our patients was 64 ± 11 years. The sex ratio was 2.22. Hypertension and diabetes are the two most common risk factors in our population. NSTE-ACS was inaugural in almost the third of the cases. Only 7% of our patients have benefited from medical transport. In 16.20% of patients, the initial ECG found no repolarization disorder. The average delay of the first medical contact was 24.42 ± 30.25 min. The average delay for the first qualifying ECG was 30 ± 0.6 min. The average length of stay in the emergency department before admission to the cardiology department was 24.13 ± 21.33 h. More than half of our study population (68%) performed their angiograms within 48 h. During our follow-up of 500 patients, 12 patients were completely lost. Patients who presented at least one MACE were at one month: 58 patients (11.6%), at 6 months: 112 patients (22.4%) and at 1 year 136 patients (27.2%).

Conclusion: Cardiovascular disease is the leading cause of death worldwide. Assessment of our practices is important to improve prognosis. Registers offer a guarantee of methodology, and are a real mirror of our medical care.

Keywords: Acute coronary syndrome; Emergency department; Management; Delay

Introduction

Cardiovascular Disease (CVD) is the leading cause of death worldwide especially in low-income and middle-income countries. It is now admitted that there is a strong association between CVD morbi-mortality and socio-economic status. This has been attributed both to higher prevalence, poor control of cardiac risk and to unequal access to health care facilities. However, most of these studies were carried out in high income countries and only few studies from low- and middle-income countries which have the highest burden of CVD. In Tunisia, an increasing country, acute coronary syndromes: Both with and without ST segment elevations are the most interesting CVD in emergency practice. But the data according to their characteristics, management and outcomes are lacking. In this paper, we will try to analyze the epidemiological profile of patients, the strategy and the different delays for medical care of NSTE-ACS from our local register as well as their short and

long term outcomes.

It is now admitted that adherence to guidelines has been correlated with improvements in patient outcomes in ACS, including reduced mortality, improving short and long-term outcomes and so reduced health care costs [1,2].

Materiel and Methods

This is an analytical transversal study, carried out in the emergency department of SAHLOUL, relating to patients treated for NSTE-ACS during the study period from 01/01/2015 to 31/12/2016. We analyzed the data from our local Registry of Acute Coronary Syndrome (ReSCUS). In brief, this registry is a continually ongoing mono-center registry that prospectively collects information regarding all patients presenting with Acute Coronary Syndrome managed in our emergency department (STEMI and NSTE-ACS). Only data of patients with NSTE-ACS were selected for this study.

We included all patients consulting for chest pain and for whom the diagnosis of NSTE-ACS was retained according to the definition established by the European Society of Cardiology (ESC). This definition is based on clinical, electrical and biological criteria.

Non-inclusion criteria

Patients with an STMI or other etiologies of chest pain: Our primary endpoint was to identify predictors of Major cardiovascular events (mortality, recurrence of NSTMI, STEMI, and Acute Congestive Heart Failure) in short and long term. The secondary endpoint was to describe the epidemiological characteristics of these patients and the quality of medical care in emergency department. The data were collected on pre-established sheets.

Statistical analysis

All analyses were performed with the SPSS statistical software.

Results

A total of 850 patients who had presented to the emergency department of SAHLOUL for NSTE-ACS were assessed for eligibility, 12 of whom were lost to follow-up, and only 500 patients were enrolled because of the incomplete data. The average age of our patients was 64 ± 11 years. The majority of our population was over the age of 40 (99%) and patients over the age of 65 accounted for 44.8%. The sex ratio was 2.22. Hypertension and diabetes are the two most common risk factors in our population. Acute coronary syndrome without ST segment elevation was inaugural in almost the third of the cases (40.6%). A history of NSTE-ACS is found in (41.8%). Revascularized myocardial infarction was found in 17.6%. Twenty-two patients had a history of chronic kidney disease (4.4%). Five of our patients had a history of ischemic stroke or obliterating arterial disease of the lower limbs. Only 7% of our patients have benefited from transportation by the mobile emergency and resuscitation service team, while the majority: 93% were taken to the emergency department by their own means of transport or by a category B ambulance. In our study population 67% (N=335) of our patients had a chest pain score between 2 and 4, hence considered to be of intermediate risk and 33% (N=165) had a chest pain score ≥ 5, therefore considered to be of high risk and none of our patients were of low risk (Score <2). Regarding the TIMI risk score, 20.2% were in group 1 (TIMI score: 0 to 2, low risk), 41.4% were in group 2 (TIMI score: 3 to 4, intermediate risk) and 38.4% were in group 3 (TIMI score: 5 to 7, high risk). For 81 patients (16.20%) the initial ECG found no repolarization disorder. The mean initial glucose level was 10.31 mmol/L ± 5.2 with a median

of 8.5 mmol/L (6.5 to 12.5). The mean initial creatinine level was 95.93 meq/l ± 60.07 with a median of 81 (69-100.5). For cardiac ultrasound data, all the patients included in the study underwent a cardiac ultrasound after their admission to the cardiology department on the second or third day of their hospitalization. The majority of our patients (95.5%) had an ejection fraction >40% and 12 patients (2.4%) had an ejection fraction ≤ 40% (12 patients were lost to follow-up). All the patients included in this study received triple anti-ischemic therapy: two platelet aggregation inhibitors: 250 mg (Aspirin), clopidogrel 300 mg or 75 mg for patients over 75 years and

Table 1: Clinical and demographic characteristics of the population.

Age	64 ± 11 ans	
Gender	Male	69%
	Fe male	31%
Risk factors	Hypertension	56.6%
	Diabetes	50.2%
	Smoking	41.6%
	Dyslipidemia	23.4%
coronary history	None	40.6%
	ACS non STEMI	41.8%
	ACS STEMI	17%
Other antecedents	Renal failure	4.4%
	Stroke/ arteriopathy of the lower limb	0.2%
Mode of transport	The Mobile Emergency and Resuscitation Service	7%
	Type B Ambulance or by their own means	93%
Chest pain Score	Between 0 et 1	0%
	Between 2 et 4	67%
	More than or equal to 5	33%
TIMI Risk Score	Between 0 et 2	20.2%
	Between 3 et 4	41.4%
	More than or equal to 5	38.4%
ECG data	Normal	16.2%
	ST segment depression	66.8%
	Negative T wave	19%
Biomarkers: Troponin	Troponin 1	0.12 (0.04-0.5)
	Troponin 2	0.35 (0.07-1.32)
	Delta troponin	0.1 (0-0.85)
Biology	Creatinin	95.93 meq/l ± 60.07
	Glycemia	10.31 mmol/l ± 5.2
Echocardiographic data	Ejection Fraction >40%	95.5%
	Ejection Fraction ≤ 40%	2.4%
Treatment	DL-LYSINE ACETYLSALICYLATE 250 mg	100%
	Clopidogrel 300 mg or 75 mg	100%
	Heparin	100%
Orientation	Admission to a cardiology department	98.2%
	Home discharge	1.8%
Angiographic data	Monotruncular involvement	47.8%
	Bitruncular involvement	12.4%
	Tritruncular involvement	6.4%
	Normal angiography	33.4%

Table 2: Major cardiovascular events in short and long term.

Major Acute Cardiovascular Events (MACE)	01 month	06 month	01 year
Total rate	11.6%	22.4%	27.2%
Lost to follow up	2.4%	-	-
Mortality at one month	0.8%	2.3%	3.4%
Myocardial infarction	4.4%	3.2%	1.2%
Anginal reccurence	5%	10%	15.8%
Acute congestive heart failure	1.4%	5.6%	6.8%

Table 3: Time delay of in hospital care.

Time from the occurrence of chest pain to arrival at the first care facility	248.7 ± 212.09 mn
Time of first time contact	24.42 ± 30.25 min
Time to qualifying ECG	30 min ± 0.6
length of stay in emergency department	24.13 hours ± 21.33
Time to perform angiography/angioplasty	<48 h (68%)
	48 h - 7 h (24.4%)
	>7 h (7.6%)

an anticoagulant: Unfractionated heparin (NFH) 50 mg, then Low Molecular Weight Heparins (LMWH) 1 mg/kg (twice a day) with systematic adjustment of doses according to age and renal function (Table 1).

Most of our patients (98.2%) were transferred to the cardiology department, (1.8%) were referred to the outpatient cardiology department. The average time between the onset of pain and the patient's arrival at the first medical care was 248.7 ± 212.09 min. In our study, 51% consulted between 2 and 6 h and only 26.6% consulted within 2 h after the start of chest pain. The average delay between the time the patient arrived in the Emergency Room (ER) and the first medical contact at the triage unit was 24.42 ± 30.25 min (ranging from 0 min to 295 min). The average time to have the 1st qualifying ECG was 30 ± 0.6 min. The average length of stay in the ER before admission to the cardiology department was 24.13 ± 21.33 h and a median of 18 h (Table 2, 3). The coronary status of patients undergoing angiography was: Mono-trunk involvement in 47.8%, bi-trunk involvement in 12.4%, tri-trunk involvement in 6.4% but in 33.4% the angiography was normal (or infiltrated networks without significant stenosis). The MACE rate at 30 days 6 and 12 months is shown in the Table 2. During our follow-up of 500 patients 12 patients were completely lost to follow-up. At 1 month, 58 (11.6%) patients presented with MACE, four (0.8%) patients had died, 22 (4.4%) patients had an MI, anginal recurrence was observed in 25 (5%) patients and seven (1.4%) of the patients had an acute edema of the lung/a congestive heart failure. At 6 months, 112 (22.4%) had MACE, only 14 (2.8%) patients had died, 16 (3.2%) patients had suffered from a myocardial infarction. The most common MACE was recurrent ACS ST-, from which 54 (10.8%) patients had suffered and 28 (5.6%) of patients presented acute heart failure. At 1 year, 136 (27.2%) patients had MACE, 17 (3.4%) patients died, 6 (1.2%) patients had a myocardial infarction, 79 (15.8%) patients had recurrent acute coronary syndrome and 34 (6.8%) patients presented acute heart failure. The main risk predictors for the occurrence of MACE was TIMI Risk SCORE >3, chest pain SCORE, age ≥ 65 years and a history of coronary artery disease (Table 4). The rate of MACE according to time from the occurrence of chest pain to arrival at the first care facility is represented in Table 5. Table 6 represents the rate of MACE according to time of first medical

Table 4: Predictors of MACE in one year of follow-up.

Predictors of MACE	P	OR CI [95%]
Age ≥ 65 years	<0.001	2.514 [1.744-3.625]
Renal failure	0.007	3.783 [1.353-10.579]
Diabetes	0.011	1.592 [1.112-2.279]
Dyslipidemia	0.009	1.745 [1.146-2.657]
Hypertension	0.050	1.423 [0.991-2.044]
History of bypass/ Angioplasty	0.002	1.771 [1.232-2.546]
TIMI Score >3	<0.001	2.745 [1.680-4.485]
Chest Pain Score	<0.001	3.014[1.950-4.657]
History of coronary disease	0.001	1.819 [1.256-2.634]

Table 5: Rate of MACE according to time from the occurrence of chest pain to arrival at the first care facility.

		MACE	No MACE	P
Duration (min)	Average	239.9 ± 197.9	258.6 ± 225.2	0.335
	Median	180 [99.5-333.7]	195.5 [118.7-337.5]	
Delay (min)	<120 min	63	66	
	120-360 min	108	141	0.587
	>360 min	51	59	

Table 6: Rate of MACE according to time of first medical contact.

		MACE	No MACE	P
Duration (min)	Average	20.83 ± 20	26.71 ± 35	0.029
	Median	15 [5-30]	15 [5-31]	
Delay	<10 min	71	94	
	10-30 min	115	105	0.011
	>30 min	36	67	

Table 7: Rate of MACE according to time to perform angiography/angioplasty.

		MACE	No MACE	P
Duration (days)	Average (DS)	3.29 ± 5.83	2.89 ± 5.66	0.447
	Median (IQR)	2 (0-3)	1(0-3)	
Delay	≤ 48 h	152	181	0.920
	>48 h	70	85	

contact. And finally the rate of MACE according to time to perform angiography/angioplasty was represented in the Table 7.

Discussion

The average age, in the French FAST-MI 2015 register, was 68 ± 14 years. According to Eisenmann et al. [3] age is an important risk factor for cardiovascular disease. The epidemiology of our population is also similar, in our study the average age is 64 ± 11 years. In western countries, hypertension is the first cardiovascular risk factor found in patients suffering from coronary disease: 24% in the USA while in our results this prevalence was 56.6% [4]. For diabetes, numerous studies have concluded that patients with diabetes presented more frequently tritruncular involvement with an often poor quality downstream bed. In our series, 50.2% of patients were diabetic. Thus, the majority of Tunisian studies indicate the high prevalence of this risk factor. The United Kingdom Prospective Diabetes Study (UKPDS) was the largest study interested in diabetic patients. In this study, conducted between 1977 and 1991, including 5,102 patients aged from 25 to 65 years with type 2 diabetes, according to the criteria of the American Diabetic Association, have been followed for 20 years. It

has thus been shown that coronary artery disease is the main cause of death in type 2 diabetes and 11% of patients developed myocardial infarction or angina over a median of 8 years [5]. In our study, the average consultation time was 249 min. This delay is relatively long compared to those observed in the European, North American and Middle Eastern registers. We found a delay of 145 min in the European Heart Surveys 2,150 min in the SPACE register [6,7], and 180 min in the PRAISE-UK register [8-10]. This can be improved by raising public awareness so that they consult as soon as possible in the event of chest pain, especially in the presence of cardiovascular risk factors. The HAS recommends a delay less than thirty minutes [11]. In our study, the average time for triage was 24.42 min. There was a significant difference between the group with MACE and the group without MACE during one year of follow-up with a P=0.029 but no significant difference between the group of survivors and the group of non survivors. It is recommended to do an ECG within 10 min of the first medical contact [12]. In our study, this delay is 30 min.

In our study 68% of patients had their angioplasty done in less than 48 h. Experts noted that the decision to invasive or conservative strategy of NSTE-ACS and the timing of angiography is based on the patient's risk stratification.

According to the AHA recommendations, an invasive strategy is indicated within 72 h after the onset of symptoms in the presence of a criterion of high risk and/or recurrence of symptoms (Grade I-A). In case of very high ischemic risk (refractory angina, acute heart failure, threatening ventricular disorders, hemodynamic instability), a coronary angiography must be performed within 2 h (Grade I-C). In addition, an early invasive strategy (<24 h) is recommended in the event of a GRACE score >140 or in the presence of at least one high risk criterion (Grade I-A) [13]. If we follow the ESC recommendations, an invasive strategy, when decided, should be completed within 72 h. By comparing ourselves to the recommended deadlines, our results are generally satisfactory, regardless of the risk of our patients.

Conclusion

The objectives of this work were the assessment of our practices compared to those recommended and the assessment of short and long-term prognosis regarding major cardiovascular events. The statistical analyzes carried out in our study do not allow us to establish a causal link between most of the risk factors and mortality or MACE. There is an urgent need for a national register to generalize our results and compare them with international registers for evaluation. Efforts remain to be made to improve our overall management of NSTE-ACS and to further improve the long-term prognosis of our patients.

Interests and Limitations

Our study is subject to several limits: It is a single-center study, not consecutive. Our observations relate to the practices observed, within the Emergency Department of Sahloul University Hospital and a large group of patients were excluded because incomplete data.

References

1. Smith FG, Brogan RA, Alabas O, Laut KG, Quinn T, Bugiardini R, et al. Comparative care and outcomes for acute coronary syndromes in Central and Eastern European transitional countries: A review of the literature. Eur Heart J Acute Cardiovasc Care. 2015;4(6):537-54.

2. Rapsomaniki E, Thuresson M, Yang E, Blin P, Hunt P, Chung S-C, et al. Using big data from health records from four countries to evaluate chronic disease outcomes: A study in 114 364 survivors of myocardial infarction. Eur Heart J Qual Care Clin Outcomes. 2016;2(3):172-83.

3. Eisenmann JC, Malina RM. Age-related changes in subcutaneous adipose tissue of adolescent distance runners and association with blood lipoproteins. Ann Hum Biol. 2002;29(4):389-97.

4. Ben Romdhane H. Les cardiopathies ischémiques, l'épidémie et ses déterminants - Vol. 1: Les facteurs de risque. Tunis: Institut National de Santé Publique. 2001. p. 317.

5. Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). UK Prospective Diabetes Study (UKPDS) Group. Lancet. 1998;352(9131):837-53.

6. Mandelzweig L, Battler A, Boyko V, Bueno H, Danchin N, Filippatos G, et al. The second Euro Heart Survey on acute coronary syndromes: Characteristics, treatment, and outcome of patients with ACS in Europe and the Mediterranean Basin in 2004. Eur Heart J. 2006;27(19):2285-93.

7. Alhabib KF, Hersi A, Alfaleh H, Alnemer K, Alsaif S, Taraben A, et al. Baseline characteristics, management practices, and in-hospital outcomes of patients with acute coronary syndromes: Results of the Saudi Project for Assessment of Coronary Events (SPACE) registry. J Saudi Heart Assoc. 2011;23(4):233-9.

8. Collinson J, Flather MD, Fox KA, Findlay I, Rodrigues E, Dooley P, et al. Clinical outcomes, risk stratification and practice patterns of unstable angina and myocardial infarction without ST elevation: Prospective Registry of Acute Ischaemic Syndromes in the UK (PRAIS-UK). Eur Heart J. 2000;21(17):1450-7.

9. Taneja AK, Collinson J, Flather MD, Bakhai A, de Arenaza DP, Wang D, et al. Mortality following non-ST elevation acute coronary syndrome: 4 years' follow-up of the PRAIS UK Registry (Prospective Registry of Acute Ischaemic Syndromes in the UK). Eur Heart J. 2004;25(22):2013-8.

10. Collinson J, Perez de Arenaza D, Flather MD, Bakhai A, Adgey AA, Fox KA, et al. Managing high-risk patients with acute coronary syndromes: The Prospective Registry of Acute Ischaemic Syndromes in the UK (PRAIS-UK). Clin Med (Lond). 2004;4(4):369-75.

11. HAS. Elaboration de recommandations de bonne pratique. 2010.

12. Roffi M, Patrono C, Collet JP, Mueller C, Valgimigli M, Andreotti F, et al. 2015 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation. Task Force for the management of acute coronary syndromes in patients presenting without persistent ST-Segment Elevation of the European Society of Cardiology (ESC). Eur Heart J. 2016;37(3):267-315.

13. Amsterdam EA, Wenger NK, Brindis RG, Casey DE Jr, Ganiats TG, Holmes DR Jr, et al. 2014 AHA/ACC guideline for the management of patients with non-ST-elevation acute coronary syndromes: Executive summary: A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Circulation. 2014;130(25):2354-94.