

**Epidemiology
of Acute Coronary Syndromes
in Cypriot Population**



CYPACS Study

**Cyprus Study of
Acute Coronary Syndromes**

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FORWARD BY THE MINISTER OF HEALTH

«EPIDEMIOLOGY OF ACUTE CORONARY SYNDROMES IN CYPRIOT POPULATION»

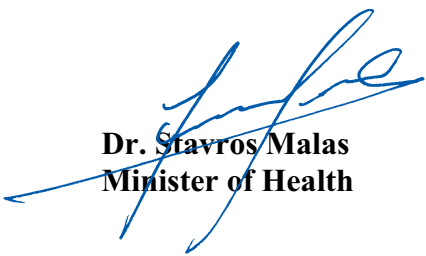
It is known that national strategies planning for medical prevention and management of coronary artery disease in 21st century, should take into account the published international, as well as local research data.

The epidemiological study of Acute Coronary Syndromes in Cypriot population is a reliable source of scientific and epidemiological data for our country. These data urge us to plan a National Strategy, not only dealing with factors predisposing to coronary artery disease, but also dealing with a more effective management of patients who present with an Acute Coronary Syndrome.

The results of the present study by L. Antoniadis et al. classify Cyprus in about the average of European countries, as far as the prevalence of Acute Coronary Syndromes is concerned. This indicates that the messages and warnings by the scientific community and the Ministry of Health have been passed on to the population in a positive manner. However, since health does not constitute a disputable good, the efforts to keep prevention as a main purpose for the function of our Welfare, should continue informing and educating our citizens on health matters.

We consider the scientific community as a precious partner for the planning and implementation of health policies. The present study should be considered as a cornerstone one for Cypriot health issues and we, as the Ministry of Health encourage conduction of further research and keep informing and educating not only the whole scientific community but our population as well.

It is a great honour for me to address this booklet and to emphasise the devotion of the researchers and their partners in conducting such an important scientific work in Cyprus.



Dr. Stavros Malas
Minister of Health

PROLOGUE

To my great satisfaction, I studied the detailed Epidemiological registry and analysis of Acute Coronary Syndromes on the Cypriot population which was organized under the scientific responsibility of Dr. Loizos Antoniadis in cooperation with relevant scientific bodies.

This registry is of inestimable value, as it brings forward data and parameters necessary to contemporary cardiovascular medicine while contributing to effective Health Services Planning through its codification of events and subsequent analysis.

Respective registries are highly appreciated by the European Society of Cardiology and National Health Societies that often encourage such efforts, since Europe as a whole is in need of reliable data in order to organize effectively current and future needs and priorities.

As President of the European Society of Cardiology, and also as an honorary member of the Cyprus Society of Cardiology, I wish to congratulate Dr. Antoniadis and the cooperating bodies on their exceptional work.

Professor Panos Vardas

A handwritten signature in blue ink, appearing to read 'P. Vardas', with a stylized flourish at the end.

President of the European Society of Cardiology

PREFACE BY THE SCIENTIFIC COORDINATOR

Cardiovascular diseases constitute the main cause of increased morbidity and mortality in the developed and developing countries of the world. The most important expression of cardiovascular diseases is coronary artery disease and its consequences. Acute Coronary Syndromes (ACS) constitute the most dramatic expression of coronary artery disease. Due to the fact that ACS are defined by certain diagnostic criteria, they are frequently used in epidemiological studies for the assessment of the prevalence of coronary artery disease across a country population. The knowledge of the clinical and epidemiological characteristics of ACS contributes in an accurate planning of the treatment, as well as prevention of coronary artery disease.

In Cyprus the morbidity of ACS has not been extensively studied. The prevalence of ACS, their predisposing factors and the treatment of these patients remain to an extent unknown. The present study has been undertaken for the investigation of epidemiological characteristics of patients presenting with an ACS in Cypriot population, exclusively in the Nicosia province which is the largest district of Cyprus.

We trust that the results of this study will provide the Cypriot medical community with valuable information regarding the epidemiological characteristics of ACS. The study will also provide the Ministry of Health and other Scientific Societies valuable information for creating an effective national strategic plan for better prevention and treatment of ACS.

At this point I would like to express our appreciation to the Minister of Health Dr. Stavros Malas for addressing the study. I would also like to thank Professor of cardiology Dr. Panos Vardas, President of the European Society of Cardiology, for the honour of introducing the study. I would like to express many thanks to the General Director of the Ministry of Health Mr. Dionysios Mavronicolas and the senior officer of the Ministry of Health Mr. Theodosios Tsiolas for support provided to us.

Additionally, I would like to thank Director of Cardiology Department at Nicosia General Hospital, Dr. Evagoras Nicolaides, for his unconditional support throughout the present study. Deep appreciations to the researches, Theodoros Christodoulides MD, Panagiota Georgiou MD, Christina Hadjilouka MD, Evi Christodoulou MD and Elias Papasavas MD, who devoted themselves in this study and worked hard for its completion. Finally I wish to express my appreciation to Dr. Andreas Papavasiliou for the detailed language supervision, to Dr. Michael Myrianthefs MD for his constructive comments and last but not least Mr Christos Anastasiades and Dr. Evros Demetriades for the assessment of the statistical results.



Loizos Antoniadis
MD, PhD, FESC, FACC

Epidemiology of Acute Coronary Syndromes in Cypriot population

CYPACS Study, Cyprus Study of Acute Coronary Syndromes

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INTRODUCTION

Acute Coronary Syndromes (ACS) are a major cause of death and disability in the developed countries of the world. Current efforts are aiming for prevention, as well as for timely and effective treatment. Knowledge of epidemiological and clinical characteristics of ACS is of critical importance in order to evaluate the cause of the problem. It is also required in order to effectively design strategies for the treatment and prevention of the problem.

Several Epidemiologic studies from European countries,¹⁻¹⁰ have investigated the etiologic complex of coronary artery disease and ACS and have led to important conclusions regarding the prevalence, the type of presentation and the treatment of ACS in western Europe. They have also offered important information regarding social, economical, and demographic characteristics of such patients, their nutrition habits, the level of activity, their psychological profile, as well as the prevalence of known risk factors for coronary artery disease. The epidemiological characteristics of ACS patients have been confirmed by many of the above mentioned studies.

It has been shown by recent epidemiologic studies and registries in European countries, during the years 2007-2008,¹⁻¹⁰ that the annual incidence of ACS in Europe is 90-312 Acute Coronary Syndromes per 100 000 inhabitants. According to the above studies, the incidence of ACS varies significantly between different countries. The GREECS study,⁶ which was conducted in Greece, where life and nutritional habits are close to

Cyprus, studied the epidemiological characteristics of patients who were admitted for ACS in one urban and five rural hospitals of Greece, from October 2003 to September 2004, has shown an annual incidence of 226 ACS per 100 000 inhabitants.

The HELIOS⁷ study which took place in 2005-2006 covering a large part of Greece, recorded an average of 185 admissions for ACS per 100 000 inhabitants yearly. One hundred and ten of those admissions were patients with ST-elevation myocardial infarction (STEMI). In nearby countries (Israel and Turkey), which have different life-styles and nutritional habits, the incidence of ACS was 136 and 312 per 100 000 people, respectively.¹⁰

No large studies have been performed so far in Cyprus, therefore data regarding epidemiology and treatment of ACS in Cyprus are scarce. Small studies which were performed during 1990-1996 have shown that the annual incidence of acute myocardial infarction in the area of Nicosia was around 140 per 100 000 inhabitants.¹¹⁻¹³ A study in the area of Larnaca in 2005¹⁴ has shown an annual incidence of 198 ACS per 100 000 people. The actual incidence of ACS in the Cypriot population has not been extensively studied. There is also lack of evidence regarding social and demographic characteristics of ACS patients, their nutritional habits, their level of activity and education, their psychological profile regarding depression, as well as the prevalence of coronary artery disease risk factors.

The aim of the present study was to record the annual incidence of ACS in the area of Nicosia, the largest district of Cyprus and to study their epidemiological characteristics, based on a protocol which was initially used in the GREECS⁶ study. Specifically, the prevalence of coronary artery disease risk factors, clinical and laboratory characteristics as well as treatment of ACS patients was studied.

The secondary targets of the study were the personal and social characteristics which might be related to ACS, such as family status, level of education, type of work and whether the patient was living in a rural or an urban area. The level of activity, depression, and nutrition habits in relation to the Mediterranean diet, were also studied.

The final goal of the study was to record and reveal the national reality regarding the incidence, prevention, and treatment of ACS in Cyprus. The results of the study should be a valuable tool for the Ministry of Health, the scientific societies, and other health organizations, in assisting them to plan

the national strategy for prevention through treatment of risk factors and for treatment of patients suffering from an ACS.

STUDY DESIGN, MATERIAL AND METHODS

Study material and population

All patients who were included in the study were residents of Nicosia province, which is the largest district of Cyprus with population of 315 400 people and were admitted for an ACS in Nicosia General Hospital for a period of 12 months, from January to December 2009. Patients transferred from another province and patients who were residents of another province besides Nicosia, were excluded from the study.

The population of patients with acute coronary syndrome across Cyprus was considered homogeneous, therefore the results from Nicosia province can be considered as representative of the whole of ACS in Cyprus.

Study protocol

The study protocol was similar with the one used in the GREECS⁶ study of the First Cardiology Clinic, School of Medicine, University of Athens and the Department of Nutrition – Dietetics, Harokopio University of Athens, Greece, with the exception of some modifications in order to be adjusted to the Cypriot population. After informing the patients and taking their consent, their medical files were used to gather information regarding the admission, demographic data, social characteristics, family status, in-hospital course and treatment of the patients.

Inclusion criteria

The inclusion criteria of the study were: (a) admission to Nicosia General Hospital with the diagnosis of ACS and (b) permanent residency in Nicosia province. Patients with ACS were considered those who fulfilled at least two of the three following diagnostic criteria: (1) acute chest pain, (2) electrocardiographic changes of the ST/T segment (persistent or non-persistent ST elevation or other ST changes) and (3) increase in myocardial necrosis biomarkers (troponin I > 0.4ng/ml and/or CPK-MB > 8.8 ng/ml).

Clinical and laboratory characteristics of the study population

Information concerning the patients' personal and family history was included in the study protocol. Specifically, family history of early coronary artery disease (men < 55 years old and women < 65 years old), hypertension and hyperlipidemia were recorded. Regarding personal medical history, the pre-existence of coronary artery disease, coronary intervention or by-pass

surgery were recorded. The presence of hypertension, hyperlipidemia, diabetes mellitus, obesity and smoking habits were also investigated.

Hypertensive patients were defined as those with blood pressure readings above 139/89 mmHg, or those receiving anti-hypertensive treatment. Hyperlipidemia was defined as total cholesterol >190 mg/dl (or >175 mg/dl for patients with history of coronary artery disease or diabetes mellitus) or treatment with hypolipidemic drugs. Diabetes was defined as fasting blood sugar >110 mg/dl (>6 mmol/L).

The admission diagnosis was based on electrocardiographic changes and myocardial necrosis biomarkers. Patients were classified in three categories of ACS according to the European Society of Cardiology guidelines.¹⁵ [A] acute coronary syndrome with persistent ST-elevation (STEMI: ST elevation myocardial infarction). [B] patients with ACS without ST-elevation (NSTEMI-ACS, non ST-elevation ACS), were classified according to the presence or not of high troponin levels to: [B1] myocardial infarction without persistent ST-elevation (NSTEMI: non ST-elevation myocardial infarction) and [B2] unstable angina.

Finally, according to the hospitalization records, the initial reperfusion treatment, the in-hospital course, whether coronary angiography was performed and subsequent treatment with coronary angioplasty (PCI) or coronary artery by-pass grafting (CABG), were recorded.

Demographic and social characteristics of the patients

Age, sex, family status, living in a rural or an urban area, occupation, and education level, were recorded among demographic characteristics.

Body mass index and obesity

Body Mass Index (BMI) was defined using the height and weight of the patients. According to the World Health Organization, patients with BMI >29.9 kg/m² were considered as obese and those with BMI: 25-29.9 kg/m² were considered as overweight.

Smoking habit

Patients were classified in current smokers, passive smokers and non-smokers. Current smokers were defined those who smoked at least one cigarette daily. Ex-smokers were defined as those who quit smoking for at least 12 months. As passive smokers were considered those who were exposed to cigarette smoking for at least 30 minutes, at least three times weekly, either in their work environment or in their home.

Level of activity, nutritional habits and depression

The record of activity level,¹⁶ nutritional habits¹⁷ and depression¹⁸ was based on the GREECS study protocol.⁶

Discharge medications

The medical treatment prescribed on discharge of ACS patients was studied, in order to investigate the compliance with the guidelines of the European Society of Cardiology.¹⁵ Specifically, the prescription of aspirin, statins, clopidogrel, ACE-inhibitors, angiotensin receptor inhibitors, aldosterone inhibitors and other medications indicated after an ACS, was recorded.

Statistical analysis

The statistical analysis was performed using EXCEL and IBM PASW (Chicago Il, USA) statistics package. Descriptive analysis and inferential analysis were performed for all variables of the study.

The dispersion was calculated and frequency tables were created according to the type of the variable. For quantitative variables, the mean value and the standard deviation were calculated, while categorical values were presented with the relative and absolute frequencies. Statistical tests were used to measure and assess the results, including proportion, chi-square test and Fisher's exact test for categorical variables and t-test and dispersion analysis (anova) for quantitative values. Bonferroni multiple comparisons were used for testing percentage variables. A 95-99% confidence interval was used for all cases.

The study was approved by our clinic's scientific committee for medical research, and was performed according to the declaration of Helsinki (1989) of World Medical Association.

RESULTS

From January until December 2009, 408 patients with an ACS were enrolled, 356 were men (87.3%) and 52 were women (12.7%). The ratio of men to women was 6.8 to 1.

Age and Sex distribution of Acute Coronary Syndrome patients

The mean age of men was 62.28±12 while the mean age of women was 70.27±12 ($P<0.001$). The distribution of the patients according to age and sex is shown on Table 1 and Figure 1. Two percent (2%) of patients were under 40 years old, 9.6% were 40-49 years old, 30.1% were 50-59 years old, 25.7% were 60-69 years old, 21.8% were 70-79 years old, and 10.8% were >80 years old. The highest percentage of patients with ACS was recorded in the 50-59 years old group.

Table 1: Age and Sex distribution of Acute Coronary Syndrome patients (%)

Age	Total	Men	Women	P-value
< 30	0.5	0.3	1.9	
30-39	1.5	1.7	0.0	
40-49	9.6	10.1	5.8	0.16
50-59	30.1	33.4	7.7	<0.001
60-69	25.7	27.0	17.3	0.07
70-79	21.8	18.3	46.2	<0.001
> 80	10.8	9.3	21.2	<0.005
Total	100.0	100.0	100.0	

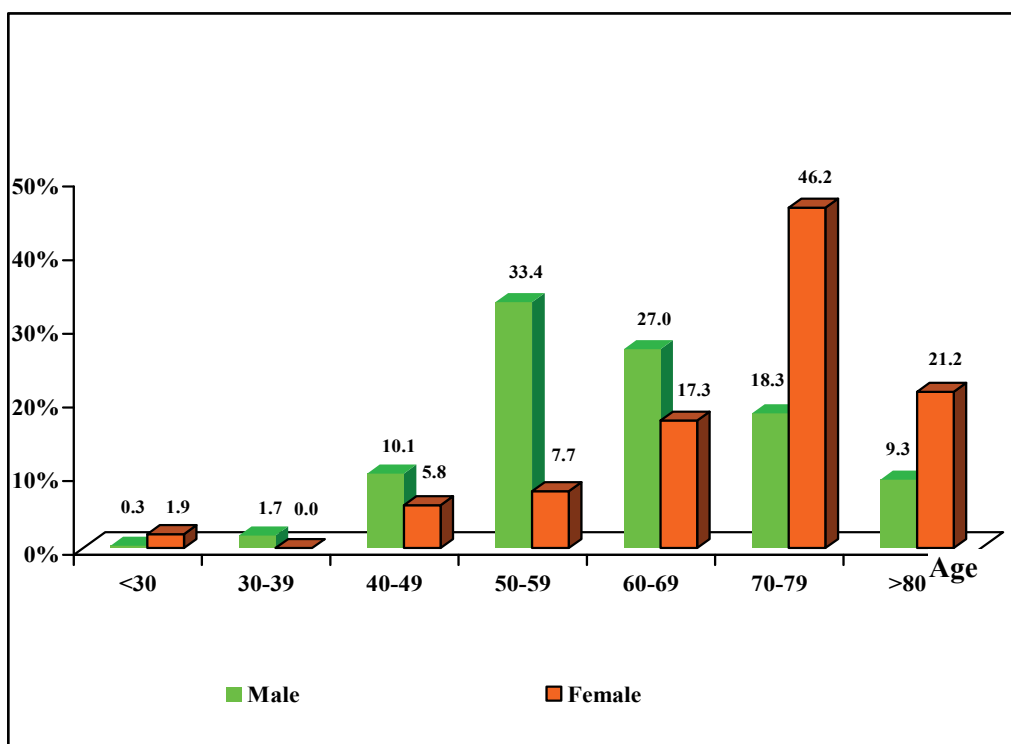


Figure 1. Distribution of Acute Coronary Syndrome patients according to age and sex.

Among men with an ACS, 2% were <40 years old, 10.1% were 40-49 years old, 33.4% were 50-59 years old, 27.0% were 60-69 years old, 18.3% were 70-79 years old, and 9.3% were >80 years old. The highest percentage of men presenting with an ACS was in the 50-59 years old group. Amongst women with an ACS 1.9% were < 40 years old, 5.8% were 40-49 years old, 7.7% were 50-59 years old, 17.3% were 60-69 years old, 46.2% were 70-79 years old, and 21.2% were >80 years old. The highest percentage of women presenting with an ACS was in the 70-79 years old group.

By comparing the age of men and women with an ACS, it was observed that men suffered from ACS, most frequently were between 50-59 years old while women were between 70 and 79 years old (Figure 1).

Annual incidence of Acute Coronary Syndromes and seasonal, monthly and daily distribution.

According to the Cyprus Statistical Service,¹⁹ the Nicosia district population in 2009, when the study was performed, had 315 400 inhabitants (156 300 males and 159 100 females). Between January and December 2009, 408 patients with an ACS were hospitalized in Nicosia General Hospital, 356 males and 52 females. The calculation of the annual incidence of ACS in Nicosia district was based on the number of all ACS patients registered for a year in the Nicosia district. In order to be more accurate in calculating the annual incidence of ACS in Nicosia district, patients who were hospitalized during the same time period at private hospitals of Nicosia, were also estimated. Information regarding those patients was gathered after interviewing the Coronary Care Units' Directors of each private hospital.

Data from private hospitals revealed that 98 patients, 85 men and 13 women, with an ACS were hospitalized during 2009 in Nicosia district's private hospitals. Based on the sum of the above data, we calculated the annual ACS incidence of Nicosia district to be 160 per 100 000 inhabitants (282 per 100 000 men and 41 per 100 000 women).

The distribution of ACS patients according to the day of admission is shown on Figure 2. Most patients were admitted during the first days of the week. 17.3% of patients were admitted on Monday, 15.9% on Tuesday, 14.4% on Wednesday, 14.4% on Thursday, 13.5% on Friday, 12.4% on Saturday and 12.1% on Sunday ($P=0.029$ between Monday and Sunday and $P=0.04$ between Monday and Saturday).

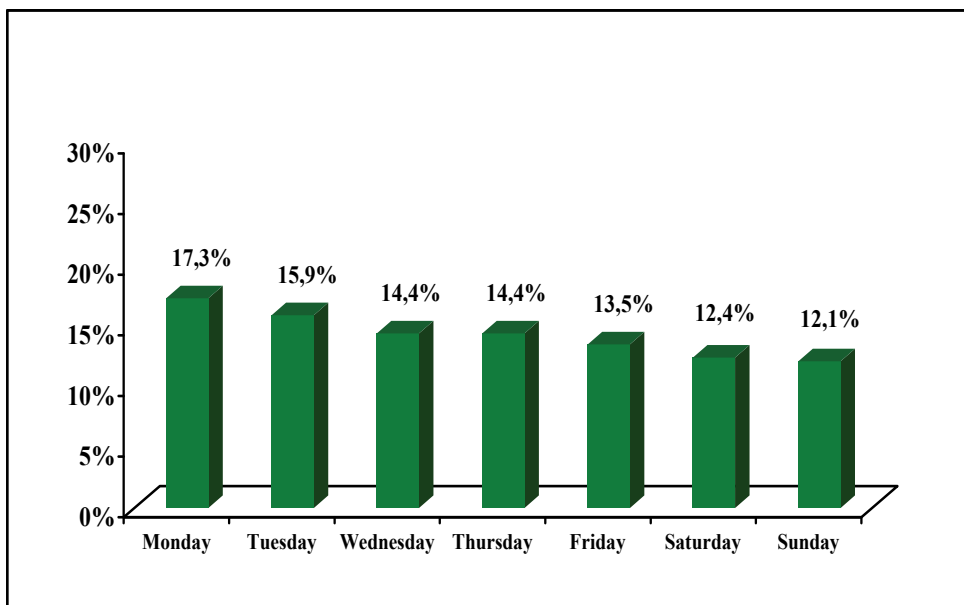


Figure 2. Distribution of Acute Coronary Syndrome patients according to the day of admission.

The distribution of ACS patients according to the month of admission is shown on Figure 3. Most admissions happened on January and December while June and July were the months with the lowest number of admissions. 10.7% of patients were admitted on January, 8.1% on February, 8.3% on March, 8.3% on April, 8.3% on May, 6.9% on June, 7.2% on July, 7.8% on August, 7.8% on September, 8.1% on October, 8.7% on November, and 9.8% on December. ($P=0.048$ between January and June).

A seasonal variation of ACS was noted by observation of the monthly distribution (Figure 4). More patients with ACS (53.2%) were admitted during colder months of the year (October-March), while 46.8% of the patients were admitted during warmer months of the year (April-September). 24.9% of patients were admitted during spring, 21.9% during summer, 24.6% during autumn and 28.6% during winter ($P=0.017$, between colder and warmer months of the year).

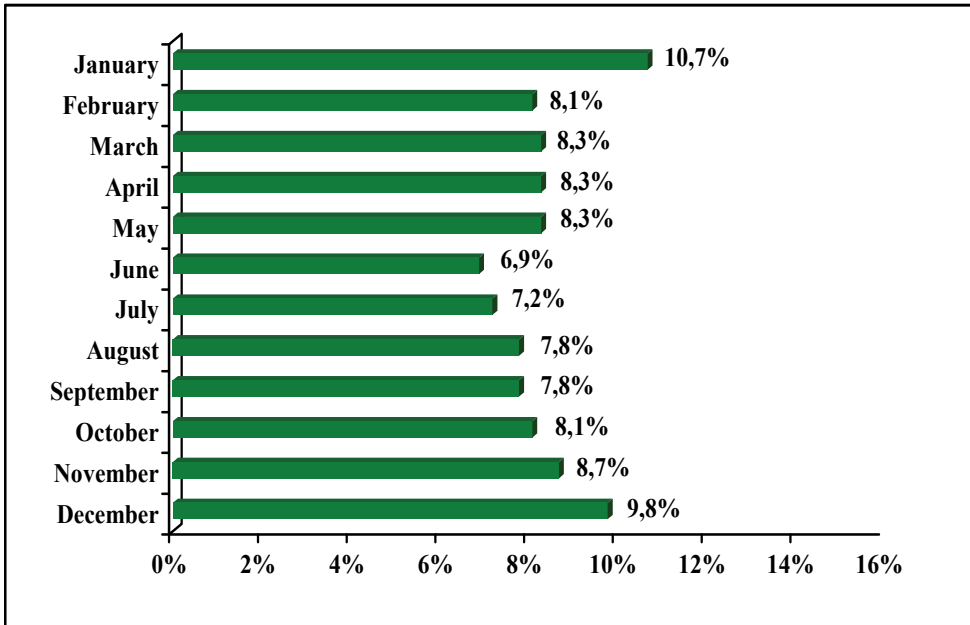


Figure 3. Distribution of Acute Coronary Syndrome patients according to the month of admission.

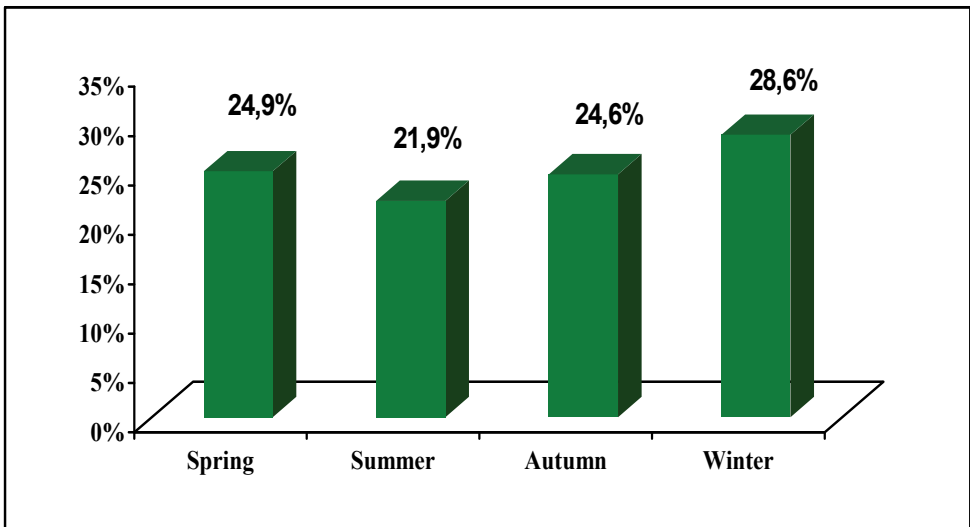


Figure 4. Seasonal distribution of Acute Coronary Syndromes

Demographic characteristics of Acute Coronary Syndrome patients

Area of living

According to the Cyprus Statistical Service (demographic report for 2009),¹⁹ among 315 400 Nicosia habitants, 236 200 were living in urban and 79 200 in rural areas of the Nicosia district. Nicosia, Strovolos, Ayios Dometios, Egkomi, Aglantzia, Lakatamia, Latsia, Anthoupoli, Tseri and Geri were defined as urban areas while the rest areas of Nicosia district were defined as rural. 74.8% of ACS patients were living in urban areas and 25.2% in rural areas. No difference was noted in the incidence of ACS between urban and rural areas (urban areas: 160 ACS per 100 000 and rural areas 159 ACS per 100 000 inhabitants, $P=NS$).

Refugees

After the Turkish invasion and occupation of the Northern part of Cyprus, a large proportion of Greek-Cypriot population (32%) became refugees. In the present study, it was found that 32.4% of ACS patients in Nicosia district were refugees while 67.6% were not. No further analysis was performed due to the lack of data regarding the exact number of refugees living in Nicosia.

Occupation and type of occupation

The classification of ACS patients according to their occupation is shown on Table 2. A percentage of 43.4% of patients were retired, 22.8% were private

Table 2: Patients with an Acute Coronary Syndrome. Classification according to occupation and sex.

Occupation	(%)		
	Total	Male	Female
Retired	43.4	39.1	74.0
Private employee	22.8	24.6	10.0
Self-employed	15.1	17.3	0.0
Government employee	12.1	13.5	2.0
Unemployed	4.8	5.5	0.0
Housewife	1.8	0.0	14.0
Total	100.0	100.0	100.0

employees, 15.1% self-employed, 12.1% government employees and 4.8% were unemployed. With regard to men: 39.1% were retired, 24.6% private employees, 17.3% self-employed, 13.5% government employees, and 5.5% unemployed. With regard to women: 74% were retired, 10% private employees, 2% government employees and 14% were housewives.

Regarding the type of occupation, 40.6% of patients were practicing manual type of work, 30% sedentary type of work and 29.4% mixed type of work. In more detail, 42.2% of men and 25.8% of women were practicing a manual type of work, while 28% of men and 48.4% of women were practicing a sedentary type of work. Finally, 29.8% of men and 25.8% of women were practicing a mixed type of work.

Level of education

Regarding the level of education, 3.7% of patients with ACS haven't attended school, 28.7% graduated primary school, 42.1% graduated from lower level high-school (Gymnasium), 20.8% from high level high school (Lyceum) and 4.7% were university graduates. Among men, 3.4% haven't attended school, 26.1% attended primary school, 43.2% lower level high-school, 22.2% upper level high-school and 5.1% graduated from colleges and universities. Among women, 5.8% did not attend school, 46.2% attended primary school, 34.6% lower level high-school, 11.5% upper level high school and 1.9% were university graduates.

Family status

Concerning family status, 78.9% of patients were married, 11.2% were widowed, 5.3% were single and 4.6% were divorced.

Physical activity

Concerning physical activity, 67.6% of ACS patients did not exercise at all, 10% were exercising 1-2 times weekly, 9.1% were exercising 3-4 times weekly and 13.2% were exercising more than 5 times per week.

Classification of patients according to the type of Acute Coronary Syndrome

As mentioned above, the type of ACS was defined according to the electrocardiographic findings and the biomarkers of myocardial necrosis (Troponin, CK-MB). Based on the above criteria, 45% of patients were diagnosed with an ST-elevation myocardial infarction (STEMI), 41.3% with a myocardial infarction without persistent ST-elevation (NSTEMI) and 13.7% with unstable angina (Table 3).

With regard to men with an ACS, 44.7% were classified as STEMI, 41% as NSTEMI, and 14.3% as unstable angina. With regard to women with an ACS, 47.1% were classified as STEMI, 43.1% as NSTEMI and 9.8% as unstable angina (Table 3).

Table 3. Patients with an Acute Coronary Syndrome. Classification according to type of syndrome and sex.

Type of Acute Coronary Syndrome	Total (%)			
	Total	Male	Female	P-value
STEMI Myocardial infarction with persistent ST-elevation	45.0	44.7	47.1	0.59
NSTEMI Myocardial infarction without persistent ST-elevation	41.3	41.0	43.1	0.92
UNSTABLE ANGINA	13.7	14.3	9.8	0.36
Total (P=0.638)	100.0	100.0	100.0	100.0

Table 4. Patients with an Acute Coronary Syndrome. Classification according to type of presentation and age.

Age	Type of Acute Coronary Syndrome			P-value *	P-value **	P-value ***
	STEMI	NSTEMI	UNSTABLE ANGINA			
< 30	1.1	0.0	0.0			
30-39	1.1	1.2	3.6			
40-49	13.2	7.1	5.4	0.05	0.05	0.32
50-59	29.7	33.4	21.4	0.43	0.22	0.08
60-69	27.5	22.4	30.3	0.26	0.33	0.22
70-79	19.2	24.1	23.2	0.26	0.51	0.89
>80	8.2	11.8	16.1	0.26	0.08	0.40
Total	100.0	100.0	100.0			

STEMI: Myocardial infarction with persistent ST-elevation.

NSTEMI: Myocardial infarction without persistent ST-elevation.

*P -value refers to comparison between STEMI /NSTEMI,

**P -value refers to comparison between STEMI/Unstable Angina

***P -value refers to comparison between NSTEMI/Unstable Angina

The distribution of ACS types according to age and sex is shown in Table 4. It is noted that among ages of 40-49 years, STEMI was the most common form of ACS ($P=0.05$ between STEMI vs NSTEMI and STEMI vs Unstable angina). NSTEMI was most common form of ACS for ages 50-59 years old ($P=0.08$ between NSTEMI and Unstable angina). In patients above 80 years old, Unstable angina was the most common type of ACS ($P=0.08$ between patients with STEMI and Unstable angina).

In-hospital treatment of patients with an Acute Coronary Syndrome

From all patients admitted with ACS, 33.6% were treated with medical reperfusion (thrombolysis), 0.7% with mechanical reperfusion (primary percutaneous coronary intervention -PCI), 6.6% with rescue PCI and 37.9% with GP IIb/IIIa receptor inhibitors (Table 5).

Table 5. In-hospital treatment of patients with Acute Coronary Syndrome

(%)

ADMISSION DIAGNOSIS	Reperfusion treatment of Acute Coronary Syndrome Patients			
	Medical Reperfusion	Mechanical Reperfusion	Rescue PCI	Use of GP IIb/IIIa
STEMI	74.4	1.6	13.7	11.7
NSTEMI	2.4	0.0	0.6	69.1
UNSTABLE ANGINA	1.8	0.0	1.8	35.4
TOTAL	33.6	0.7	6.6	37.9

STEMI: Myocardial infarction with persistent ST-elevation.

NSTEMI: Myocardial infarction without persistent ST-elevation

GP IIb/IIIa: Administration GPIIb/IIIa receptor inhibitors.

PCI: Percutaneous Coronary Intervention

In detail, 74.4% of STEMI were treated initially with medical reperfusion and 1.6% were treated with primary PCI. A rescue PCI was required for 13.7% of STEMI patients. Regarding NSTEMI 69.1% were treated with GP IIb-IIIa receptor inhibitors and 2.4% eventually received thrombolysis. Among patients with unstable angina, 35.4% were treated with GP IIb –IIIa inhibitors and 1.8% with thrombolysis.

No difference was noted in treatment with medical reperfusion between men and women (38.7% of men and 38.5% of women). 75.5% of men and 68% of women with STEMI received medical reperfusion ($P=0.36$). Regarding age, in men 66.7% of patients under 39 years old, 86.9% of patients 40-49 years old, 75.6% of patients 50-59 years old, 79.5% of patients 60-69 years old, and 63.8% of patients over 70 years old received medical reperfusion. Regarding women with STEMI, 50% of those under 49 years old, 100% of those 50-59 years old, 66.7% of those 60-69 years old and 64.3% of those above 70 years received medical reperfusion.

Coronary angiography in patients with an Acute Coronary Syndrome

Coronary angiograph:

Coronary angiography was performed in 69.1% of ACS patients during their hospitalization (Table 6), 72.8% of men and 44.2% of women ($P<0.01$). 83.3% of patients under 39 years old, 74.4% of patients 40-49 years old, 66.7% of those 50-59 years old, 73.4% of those 60-69 years old, 67.4% of patients 70-79 years old and 63.6% of patients aged over 80 years old underwent coronary angiography (Figure 5 and Table 6).

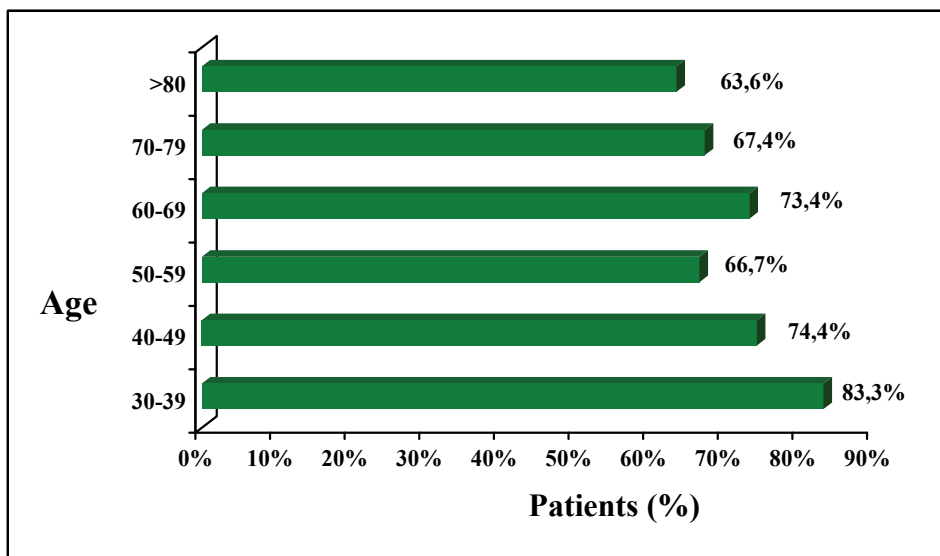


Figure 5. Percentage of Acute Coronary Syndrome patients who underwent coronary angiography. Classification according to age.

Coronary angiography was performed in 69.8% of patients with STEMI, in 72.2% of patients with NSTEMI and in 70% of patients with unstable angina. Coronary angiogram was performed in 72.6% of men and in 40% of women with STEMI ($P<0.001$), in 73.6% of men and in 45% of women with NSTEMI ($P<0.001$) and in 70.6% of men and in 60% of women with unstable angina, $P<0.04$, (Table 6).

Table 6: Patients with Acute Coronary Syndrome who underwent coronary angiography. Classification according to type of episode and sex.

(%)

Acute Coronary Syndrome	Patient undergoing coronary angiography			P-value
	Total	Male	Female	
STEMI	68.9	72.6	40.0	<0.001
NSTEMI	72.2	73.6	45.5	<0.001
UNSTABLE ANGINA	70.6	70.6	60.0	0.04
TOTAL	69.1	72.8	44.2	<0.001

STEMI: Myocardial infarction with persistent ST-elevation.

NSTEMI: Myocardial infarction without persistent ST-elevation.

Coronary angioplasty and by-pass grafting

Forty percent (40%) of patients, who underwent coronary angiography, were treated with coronary angioplasty and stent implantation on the same session, while 11% of patients were referred for coronary artery by-pass grafting (Table 7).

The percentage of men treated with PCI was higher than that of women (43.3% of men vs 17.3% of women, $P=0.008$). With PCI were treated 39% of STEMI patients (42% of men and 20% of women, $P=0.03$), 40% of NSTEMI patients (43.9% of men and 13.6% of women, $P =0.007$) and 42.9% of patients with unstable angina (45.1% of men and 20% of women, $P=0.09$) (Table 7).

Table 7. Treatment of Acute Coronary Syndromes according to coronary angiography findings (%)

TYPE OF ACS	CONSERVATIVE TREATMENT				ANGIPLASTY WITH STENT IMPLANTATION (PCI)				CORONARY ARTERY BY-PASS GRAFTING (CABG)			
	TOTAL	MALE	FEMALE	P-value	TOTAL	MALE	FEMALE	P-value	TOTAL	MALE	FEMALE	P-value
STEMI	50.6	50.4	52.0	0.325	39.0	42.0	20.0	0.036	10.4	7.6	28.0	0.02
NSTEMI	50.0	45.3	81.9	0.006	40.0	43.9	13.6	0.007	10.0	10.8	4.5	0.09
UNSTABLE ANGINA	41.0	37.3	80.0	0.005	42.9	45.1	20.0	0.009	16.1	17.6	0.0	0.11
TOTAL	49.0	46.3	67.3	0.037	40.0	43.3	17.3	0.008	11.0	10.4	15.4	0.331

STEMI: Myocardial infarction with persistent ST elevation.
 NSTEMI: Myocardial infarction without persistent ST elevation.

There was a higher percentage of women treated with CABG surgery than men (15.4% of women and 10.4% of men, $P=0.33$). In detail, 7.6% of men and 28% of women with STEMI ($P=0.02$), 10.8% of men and 4.5% of women with NSTEMI ($P=0.09$) and 17.6% of men with unstable angina, were referred for CABG ($P=0.11$). (Table 7)

Duration of hospitalization

Mean duration of hospitalization for ACS patients was 6.8 days (Median:7 Q1=6 (25%), Q2=7 (75%)). There was no significant difference between men and women regarding duration of hospital stay.

A statistically significant difference of the length of hospital stay was noted between types of ACS. Mean hospital stay for STEMI and NSTEMI was 7.6 days and 7.1 days respectively, while patients with unstable angina were hospitalized for significantly shorter duration: mean duration of hospitalization was 4.8 days, $P=0.05$ (Median:5 Q1=4 (25%), Q2=6 (75%)).

In-hospital mortality

The in-hospital mortality rate was 3.5% (3.3% for men and 4.8% for women, $P=0.435$). No deaths were recorded among patients younger than 49 years old. The mortality rate was 2.7% for patients 50-59 years old, 2.9% for 60-69 years old and 6.6% for 70-79 years old. The in-hospital mortality of STEMI was 4% and for NSTEMI 3.4% ($P=NS$). No deaths were recorded in patients with unstable angina.

Discharge medications

Medications prescribed on discharge included b-blockers, aspirin, statins, clopidogrel, ACE inhibitors, angiotensin receptor blockers, aldosterone receptor blockers as well as other medications depending on each individual (Table 8).

The medical treatment prescribed for ACS patients on discharge is shown on Table 8. B-blockers were prescribed to 68.2% of patients, aspirin to 78.4%, statin to 74%, clopidogrel to 64.2%, ACE inhibitors to 47.3%, nitrates to 35.3%, diuretics to 12%, angiotensin receptor blockers to 9.8%, calcium channel blockers to 4.7% and aldosterone antagonist to 2.9% of patients. No statistically significant differences were noted on discharge medications between men and women even though a higher percentage of women had received statins, b-blockers and clopidogrel and a higher percentage of men had received calcium channel blockers, ACE inhibitors and aldosterone antagonist.

Table 8. Medications of Acute Coronary Syndrome patients, as prescribed on discharge form.

(%)

Discharge medications	Total	Male	Female	P-value
Aspirin	78.4	78.4	78.8	0.938
Statins	74.0	73.3	78.8	0.396
B-blockers	68.2	62.9	65.4	0.731
Clopidogrel	64.2	63.5	69.2	0.419
ACE-inhibitors	47.3	47.5	46.2	0.771
Nitrates	35.3	29.8	73.1	0.001
Diuretics	12.0	12.1	11.5	0.911
Angiotensin rec. blockers	9.8	10.7	3.8	0.089
Calcium channel blockers	4.7	5.3	0.0	0.070
Aldosterone antagonists	2.9	3.1	1.9	0.642

Family and personal medical history of ACS patients

Family history of early coronary artery disease was present in 34.6% of ACS patients (34.6% of men and 34.6% of women, $P=NS$). 38.5% of the patients had a family history of hypertension (37.4% of men and 46.2% of women, $P=0.22$), 29.4% had a family history of hypercholesterolemia (30.3% of men and 23.1% of women, $P=0.28$) and 33.6% of patients had a family history of diabetes mellitus (33.1% of men and 36.5% of women, $P=0.62$) Table 9.

Personal medical history for hypercholesterolemia was positive on 49% of patients (48.3% of men and 53.8% of women, $P=0.45$). History of hypertension was present in 49% of patients (46.3% of men and 67.3% of women, $P<0.001$) and history of diabetes mellitus in 27.9% of patients (27.2% of men and 32.7% of women, $P=0.41$), Table 9. With regard to the smoking habit, 48% of ACS patients were smokers (53.1% of men and 13.5% of women, $P<0.001$), while 48.7% were passive smokers (47.7% of men and 53.8% of women, $P<0.05$).

According to body mass index, 78.4% of ACS patients weighed more than normal limits, with 54.7% being overweight (55.1% of men and 51.9% of women, $P=NS$) and 23.7% being obese (24.2% of men and 21.2% of women $P=NS$). Only 21.6% of patients were considered of normal weight (20.8% of men and 26.9% of women, $P=NS$).

By studying the prevalence of risk factors in both sexes, we observe that women presenting an ACS suffered more frequently from arterial hypertension (women:67.3% vs men:46.3% ($P<0.005$), while men suffering an ACS were more frequently smokers than women (men:53.1% vs women: 13.5%, $P<0.001$) Table 9.

Table 9. Personal medical and family history of Acute Coronary Syndrome patients. Classification according to sex.
(%)

Personal Medical and Family history	Total	Male	Female	P-value
BMI (Body Mass Index)				
Normal weight ($BMI<25 \text{ kg/m}^2$)	21.6	20.8	26.9	0.314
Overweight ($BMI>25-29.9 \text{ kg/m}^2$)	54.7	55.1	51.9	0.671
Obese ($BMI>29.9 \text{ kg/m}^2$)	23.7	24.2	21.2	0.634
Family history				
Early coronary artery disease	34.6	34.6	34.6	0.993
Arterial hypertension	38.5	37.4	46.2	0.223
Hypercholesterolemia	29.4	30.3	23.1	0.283
Diabetes mellitus	33.6	33.1	36.5	0.628
Personal medical history				
Arterial hypertension	49.0	46.3	67.3	0.005
Hypercholesterolemia	49.0	48.3	53.8	0.456
Diabetes mellitus	27.9	27.2	32.7	0.410
Smoking	48.0	53.1	13.5	0.001
Passive smoking	48.7	47.7	53.8	0.411
Previous coronary artery disease	31.6	32.9	23.1	0.156

P- value for all BMI =0.593

By studying the prevalence of risk factors in relation to age of ACS patients (Table 10), it was observed that the most common risk factor among younger ages was smoking (Age<49 years old: 68.1%, 50-69 years old: 57.9%, >70 years old: 24.1%, $P<0.001$ between <49 and >70 years old and 50-69 and >70 years old). Another frequent risk factor for younger ages was the presence of family history of coronary artery disease. (Age<49 years old: 42.6%, 50-69 years old: 38.2% and >70 years old: 25.6%, $P<0.05$ between ages <49 and >70 years old and ages 50-69 and >70 years old). In middle-ages, 50-69 years old, the most prevalent risk factors were smoking

($P < 0.001$) and hypercholesterolemia ($P = NS$), while for patients over 70 years old, the main risk factor for an ACS was arterial hypertension (Ages <40 years old: 23.4%, ages 50-69 years old: 47.4% and ages >70 years old: 60.9%, $P < 0.05$ for all age groups).

Table 10. Classification of Acute Coronary Syndrome risk factors according to age and sex.

(%)

CORONARY ARTERY DISEASE RISK FACTORS	Age groups			P-value *	P-value **	P-value ***
	<49 years	50-69 years	>70 years			
TOTAL POPULATION						
Overweight (BMI>25-29.9 kg/m ²)	51.1	54.4	56.4	0.825	0.795	0.835
Obese (BMI>29.9 kg/m ²)	23.4	25.9	20.3	0.908	0.918	0.533
Family history of early coronary artery disease	42.6	38.2	25.6	0.574	0.029	0.014
Arterial hypertension	23.4	47.4	60.9	0.003	<0.001	0.013
Hypercholesterolemia	48.9	52.6	42.9	0.644	0.471	0.073
Diabetes mellitus	6.4	26.8	37.6	0.003	<0.001	0.031
Smoking	68.1	57.9	24.1	0.195	<0.001	<0.001
MALE						
Overweight (BMI>25-29.9 kg/m ²)	53.5	54.9	56.1	0.913	0.875	0.902
Obese (BMI>29.9 kg/m ²)	23.3	26.0	20.4	0.903	0.916	0.543
Family history of early coronary artery disease	41.9	38.1	23.5	0.648	0.027	0.011
Arterial hypertension	20.9	47.4	55.1	0.001	<0.001	0.209
Hypercholesterolemia	51.2	52.1	38.8	0.911	0.171	0.029
Diabetes mellitus	7.0	26.5	37.8	0.006	<0.001	0.044
Smoking	72.1	59.5	30.6	0.122	<0.001	<0.001
FEMALE						
Overweight (BMI>25-29.9 kg/m ²)	25.0	46.2	57.1	0.453	0.203	0.612
Obese (BMI>29.9 kg/m ²)	25.0	23.1	20.0	0.836	0.805	0.875
Family history of early coronary artery disease	50.0	38.5	31.4	0.682	0.455	0.646
Arterial hypertension	50.0	46.2	77.1	0.893	0.239	0.04
Hypercholesterolemia	25.0	61.5	54.3	0.200	0.267	0.653
Diabetes mellitus	0.0	30.8	37.1	0.205	0.135	0.682
Smoking	25.0	30.8	5.7	0.825	0.170	0.02

BMI: Body Mass Index

*P - value refers to the comparison between ages < 49 and 50 - 69years old.

**P - value refers to the comparison between ages < 49 and >70 years old.

***P - value refers to the comparison between ages 50-69 and >70 years old

According to sex, the same findings as the total population were noted for men. In women over 70 years old, the most common risk factor was arterial hypertension ($P=0.04$ when comparing ages 50-69 and >70 years old), while hypercholesterolemia was the most common risk factor among women 50-60 years old ($P=NS$).

Only 9.3% of the patients did not have any one of the five most common coronary artery disease risk factors (hypertension, hypercholesterolemia, diabetes, smoking, and family history of early coronary artery disease). 21.3% of the patients had one risk factor, 32.6% had two risk factors, 25% had three risk factors, 10.8% had four risk factors and 0.5% had five risk factors. No significant differences were noted between men and women.

Considering the age of the patients, most of the patients between 40 and 49 years old had one risk factor, while older patients had two or more risk factors. Most patients with unstable angina or STEMI had two risk factors, while NSTEMI patients most commonly had three risk factors (unstable angina: 39.6%, STEMI: 32.9%, NSTEMI: 24.4%, $P=NS$).

History of a previous hospitalization for coronary artery disease was present in 31.6% of ACS patients, while for 68.4% of the patients, the hospitalization recorder was their first ever event. Among patients with previous coronary artery disease, 42.7% had a history of previous PCI, 19.7% had CABG surgery, while 7.7% had a history of both CABG and PCI. 30.2% of patients who had a history of coronary artery disease were treated conservatively.

NSTEMI was the most common form of ACS among patients with history of coronary artery disease, (NSTEMI:48.8%, STEMI:32.6%, unstable angina:18.6%, $P<0.05$ between NSTEMI, STEMI and unstable angina), while STEMI was the most common form of ACS among patients without previous coronary artery disease, (STEMI: 50.2%, NSTEMI: 38.4% and unstable angina: 11.5%, $P<0.05$ between STEMI, NSTEMI and unstable angina).

Men with history of coronary artery disease (Table 11) were presented more commonly with unstable angina (unstable angina: 45.1%, STEMI: 24.8%, NSTEMI: 37.2% $P=0.02$ between STEMI and NSTEMI, $P=0.006$ between STEMI and unstable angina and $P=0.317$ between NSTEMI and unstable angina).

Women with a history of coronary artery disease were presented more frequently with NSTEMI (NSTEMI: 36.4%, STEMI: 12%, unstable angina:20%, $P=0.049$ between STEMI and NSTEMI, $P=NS$ between STEMI and unstable angina and NSTEMI and unstable angina).

Table 11 shows the correlation between type of ACS and data from personal and family history of the patients. Men with STEMI had a family history of early coronary artery disease in 34.4% of patients, 24.8% had a history of previous coronary artery disease, 61.1% were smokers, 45.2% had hypercholesterolemia, 37.6% had hypertension and 20.4% had diabetes. Women with STEMI had family history of early coronary artery disease in 26% of patients, 12% had previous coronary artery disease, 56% were passive smokers, 52% were hypertensive, 36% were diabetic and 48% had hypercholesterolemia.

Among men with NSTEMI, 38.5% had a family history of early coronary artery disease, 37.2% had history of previous coronary artery disease, 52.7% had arterial hypertension, 53.4% hypercholesterolemia, 32.4% diabetes, and 45.9% were smokers. Women with NSTEMI had 45.4% family history of early coronary artery disease, 36.4% had history of previous coronary artery disease, 81.8% were hypertensive, 63.6% had hypercholesterolemia, 22.7% were diabetic, 9.1% were active smokers and 50% passive smokers.

Men with unstable angina had family history of early coronary artery disease in 28% of patients, 45.1% had previous coronary artery disease, 54.9% had hypertension, 43.1% hypercholesterolemia, 33.3% diabetes, and 49% were smokers. Women with unstable angina had a family history of early coronary artery disease in 40% of patients, while 20% had a history of previous coronary artery disease, 80% were hypertensive, 60% were passive smokers, 40% had hypercholesterolemia and 60% were diabetic, (Table 11).

Men with STEMI were more possibly smokers (61.1%) while women with STEMI were more commonly passive smokers (65%). Men with STEMI were more frequently smokers than men with NSTEMI (STEMI: 61.1% vs NSTEMI: 45.9%, $P=0.008$). Men and women who were smoking presented more frequently STEMI than NSTEMI. (Men: STEMI: 61.1%, NSTEMI: 45.9%: $P=0.008$, Women: STEMI: 20%, NSTEMI: 9.1%, $P=0.295$).

Among men and women with NSTEMI, the most common risk factors were hypertension (men:52.7%,women:81.8%, $P<0.05$) and hypercholesterolemia (men: 53.4%, women: 63.6%, $P=NS$).

Table 11. Correlation between type of Acute Coronary Syndrome and data from personal medical and family history of the patients. (%)

Family and Personal Medical history	STEMI	NSTEMI	UNSTABLE ANGINA	P-value*	P-value**	P-value***
<u>MEN</u>						
<u>BMI (Body Mass Index)</u>						
Normal (BMI<25 kg/m ²)	22.9	14.2	33.3	0.092	0.016	0.009
Overweight (BMI>25-29.9 kg/m ²)	53.5	58.1	51.0	0.752	0.805	0.901
Obese (BMI>29.9 kg/m ²)	23.6	27.7	15.7	0.586	0.049	0.041
<u>Family history</u>						
Early coronary artery disease	34.4	38.5	28.0	0.614	0.358	0.209
Hypertension	38.8	40.5	28.0	0.942	0.141	0.132
Hypercholesterolemia	26.1	37.0	28.0	0.05	0.851	0.276
Diabetes mellitus	28.0	39.2	36.0	0.068	0.324	0.746
<u>Personal history</u>						
Hypertension	37.6	52.7	54.9	0.008	0.029	0.486
Hypercholesterolemia	45.2	53.4	43.1	0.154	0.795	0.207
Diabetes mellitus	20.4	32.4	33.3	0.017	0.058	0.906
Smoking	61.1	45.9	49.0	0.008	0.127	0.704
Passive smoking	52.2	43.2	47.1	0.114	0.521	0.628
Previous coronary artery disease	24.8	37.2	45.1	0.02	0.006	0.317
<u>WOMEN</u>						
<u>BMI(Body Mass Index)</u>						
Normal (BMI<25 kg/m ²)	28.0	27.3	20.0	0.905	0.897	0.898
Overweight (BMI>25-29.9 kg/m ²)	44.0	59.1	60.0	0.284	0.282	0.909
Obese (BMI>29.9 kg/m ²)	28.0	13.6	20.0	0.207	0.843	0.786
<u>Family history</u>						
Early coronary artery disease	26.0	45.4	40.0	0.121	0.460	0.825
Hypertension	39.1	59.0	40.0	0.113	0.865	0.438
Hypercholesterolemia	26.0	22.7	20.0	0.898	0.807	0.895
Diabetes mellitus	26.0	54.5	20.0	0.032	0.324	0.746
<u>Personal history</u>						
Hypertension	52.0	81.8	80.0	0.031	0.249	0.925
Hypercholesterolemia	48.0	63.6	40.0	0.282	0.743	0.332
Diabetes mellitus	36.0	22.7	60.0	0.321	0.317	0.099
Smoking	20.0	9.1	0.0	0.295	0.273	0.484
Passive smoking	56.0	50.0	60.0	0.681	0.869	0.686
Previous coronary artery disease	12.0	36.4	20.0	0.049	0.631	0.484

STEMI: Myocardial infarction with persistent ST elevation

NSTEMI: Myocardial infarction without persistent ST elevation

*P-value refers to comparison between STEMI /NSTEMI

**P -value refers to comparison between STEMI/Unstable Angina,

***P –value refers to comparison between NSTEMI/Unstable Angina

Hypertension and smoking were the most common risk factors in men with unstable angina, while hypertension, diabetes and passive smoking were the most common risk factors among women with unstable angina. Hypertension and diabetes were more frequently noted among men with unstable angina (hypertension in unstable angina: 54.9% vs 37.6% in STEMI, $P=0.029$, and diabetes in unstable angina: 33.3% vs STEMI: 20.4%, $P=0.058$) Table 11.

Obese patients presented more frequently NSTEMI rather than unstable angina (NSTEMI: 27.7%, STEMI: 23.6%, unstable angina: 15.7% $P=0.04$ between STEMI and unstable angina, $P=0.04$ between NSTEMI and unstable angina and $P=0.5$ between STEMI and NSTEMI), Table 11.

Level of education, family status, nutritional habits, level of exercise and depression of patients with Acute Coronary Syndrome

Most men with an ACS were high-school graduates (43.3%), while most women graduated primary school (46.2%), Table 12. There was no statistically significant correlation between the level of education and the type of ACS, even though we observed that men with higher levels of education were more prone to present unstable angina rather than STEMI and NSTEMI ($P= NS$), Table 13.

The evaluation of family status revealed that married men had a higher possibility to suffer an ACS than married women. (men: 84.1%, women: 42.9%, $P<0.001$). Also, widowed women had a higher risk to suffer an ACS in comparison with widowed men (women: 49%, men: 5.8%, $P< 0.001$), Table 12. There was no significant correlation between family status and type of ACS, with the exception of widowed men who presented more frequently unstable angina than STEMI and NSTEMI. ($P=0.42$). Single and widowed women with an ACS had a higher risk to present with STEMI than other forms of ACS ($P= 0.75$), Table 13.

Regarding the level of activity, 66% of men and 78.8% of women with an ACS did not exercise at all, Table 12. Even if a higher percentage of men was exercising in comparison with women, there was no statistically significant difference between them ($P=0.113$). Men with a higher level of activity presented more frequently unstable angina than STEMI ($P= 0.51$), while women presented more frequently with NSTEMI ($P= 0.62$).

Table 12. Level of education, exercise and family status of patient with Acute Coronary Syndrome

(%)

Level of education, exercise, and family status of ACS patients	Total	Male	Female	P-value
<u>Level of education</u>				
Did not attend school	3.7	3.4	5.8	0.390
Primary school	28.7	26.1	46.2	0.002
Lower level high school	42.2	43.3	34.6	0.238
Higher level high school	20.8	22.2	11.5	0.008
College / University	4.7	5.1	1.9	0.316
<u>Level of exercise</u>				
No exercise	67.6	66.0	78.8	0.064
Exercising 1-2 times weekly	10.0	9.8	11.5	0.702
Exercising 3-4 times weekly	9.1	10.1	1.9	0.054
Exercising >5 times weekly	13.2	14.0	7.7	0.206
<u>Family status</u>				
Single	5.3	5.2	6.1	0.791
Married	78.9	84.1	42.9	<0.001
Divorced	4.6	4.9	2.0	0.365
Widowed	11.2	5.8	49.0	<0.001

Nutrition index was 28.1 ± 9 among ACS patients and was slightly higher, but without a statistically significant difference with regard to men compared to women (28.5 ± 9 men, 26.7 ± 5 women, $P=NS$). A higher value of nutrition index indicates a better adjustment to typical Mediterranean diet. There was no statistically significant difference of nutrition index between the types of ACS.

Depression index was 20.6 ± 8 . No statistically significant difference was noted between men and women with an ACS (men: 20.8 ± 8 , women: 19.8 ± 6 , $P=0.092$), as well as between various types of ACS (STEMI: 20.9 ± 8 , NSTEMI: 21.4 ± 8 , unstable angina: 18.7 ± 9 , $P=0.18$).

Table 13: Correlation between type of Acute Coronary Syndrome and data regarding level of education, level of exercise and family status of the patients.

(%)

Level of education, level of exercise and family status of ACS patients.	STEMI	NSTEMI	UNSTABLE ANGINA	P-value
<u>MALE</u>				
<u>Level of education</u>				0.301
Did not attend school	4.5	3.4	0.0	
Primary school	22.3	26.4	37.3	
Lower level high school	45.2	39.9	47.1	
Higher level high school	22.9	25.0	11.8	
College / University	5.1	5.4	3.9	
<u>Level of exercise</u>				0.517
No exercise	66.2	66.2	64.7	
Exercising 1-2 times weekly	10.8	8.1	11.8	
Exercising 3-4 times weekly	9.6	12.8	3.9	
Exercising >5 times weekly	13.4	12.8	19.6	
<u>Family status</u>				0.426
Single	5.9	5.6	2.0	
Married	84.2	84.6	82.0	
Divorced	5.9	4.2	4.0	
Widowed	3.9	5.6	12.0	
<u>FEMALE</u>				
<u>Level of education</u>				0.140
Did not attend school	0.0	9.1	20.0	
Primary school	40.0	50.0	60.0	
Lower level high school	32.0	40.9	20.0	
Higher level high school	24.0	0.0	0.0	
College / University	4.0	0.0	0.0	
<u>Level of exercise</u>				0.628
No exercise	76.0	77.3	100.0	
Exercising 1-2 times weekly	16.0	9.1	0.0	
Exercising 3-4 times weekly	4.0	0.0	0.0	
Exercising >5 times weekly	4.0	13.6	0.0	
<u>Family status</u>				0.751
Single	9.1	4.5	6.1	
Married	31.8	50.0	42.9	
Divorced	4.5	0.0	2.0	
Widowed	54.5	45.5	49.0	

STEMI: Myocardial infarction with persistent ST elevation

NSTEMI: Myocardial infarction without persistent ST elevation

DISCUSSION

The present study depicts the epidemiological and clinical characteristics, in addition to the in-hospital course and therapeutic approach of patients hospitalized for ACS in the Nicosia General Hospital during a period of one year, from January to December of 2009. Despite the fact that in Nicosia district also exist private hospitals, where patients with ACS are admitted, the majority of patients with ACS are admitted or referred to the Nicosia General Hospital. In spite of these limitations, the population of patients studied can be considered as representative of the cases of ACS occurring across the Nicosia district. Patients with ACS referred from other districts or inhabitants of other cities were not included in the study. As mentioned above, the population of ACS all over Cyprus is considered homogeneous and for that reason the results from Nicosia region can be considered representative of the total population of ACS in Cyprus.

Incidence of ACS in the Cypriot population

The annual incidence of ACS in the Nicosia district was calculated to 160 ACS per 100 000 habitants (1.6%). This percentage is translated in 1342 ACS episodes annually in the Cypriot population. In a previous study of ACS in the Nicosia district,¹¹ the annual incidence of acute myocardial infarctions (AMI) was 90 acute myocardial infarctions per 100 thousand habitants. In that study, patients with unstable angina were not included. If the patients with unstable angina are excluded from the population of the present study (previously unstable angina was not included in the term ACS), then the annual incidence of STEMI and NSTEMI is estimated at 140 AMI per 100 000 inhabitants, a percentage significantly increased compared to the study of 1992.¹¹ This difference could be attributed to the increase of smoking habit and the changes in the way of living the last twenty years with main characteristics being the absence of physical activity, non-healthy diet and the increasing stress of work and modern living.

In a study of ACS in thirty European countries,¹⁰ it was observed that the annual incidence of ACS varied from 90 to 312 per 100 000 habitants (Romania: 90 ACS per 100 000 habitants, Turkey: 312 ACS per 100 000 habitants). In comparison with the other European countries, the annual incidence of ACS in Cyprus was found at the mean line (Figure 6) and is significantly higher than that of France (105 per 100 000) and Belgium (114 per 100 000), is close to the incidence in Switzerland (149 per 100 000) and Bulgaria (148 per 100 000) and is slightly lower from the annual incidence of ACS in the United Kingdom (173 per 100 000 habitants). Compared to

the neighboring countries, the annual incidence of ACS is slightly higher from the incidence of ACS in Israel (136 per 100 000) but significantly lower from the annual incidence of ACS in Turkey (312 per 100 000 habitants).

In comparison with Greece, where there are similar historical and cultural habits, the annual incidence of ACS in Cyprus was found relatively lower. In the GREECS study,⁶ which was an epidemiological study of registration of ACS in one urban and five rural hospitals in Greece, the annual incidence of ACS was 226 per 100 000 habitants. In the HELIOS study,⁷ where for one year (2005-2006) all patients admitted with ACS in 31 hospitals all over Greece were recorded, the annual incidence of ACS was 185 per 100 000 habitants.

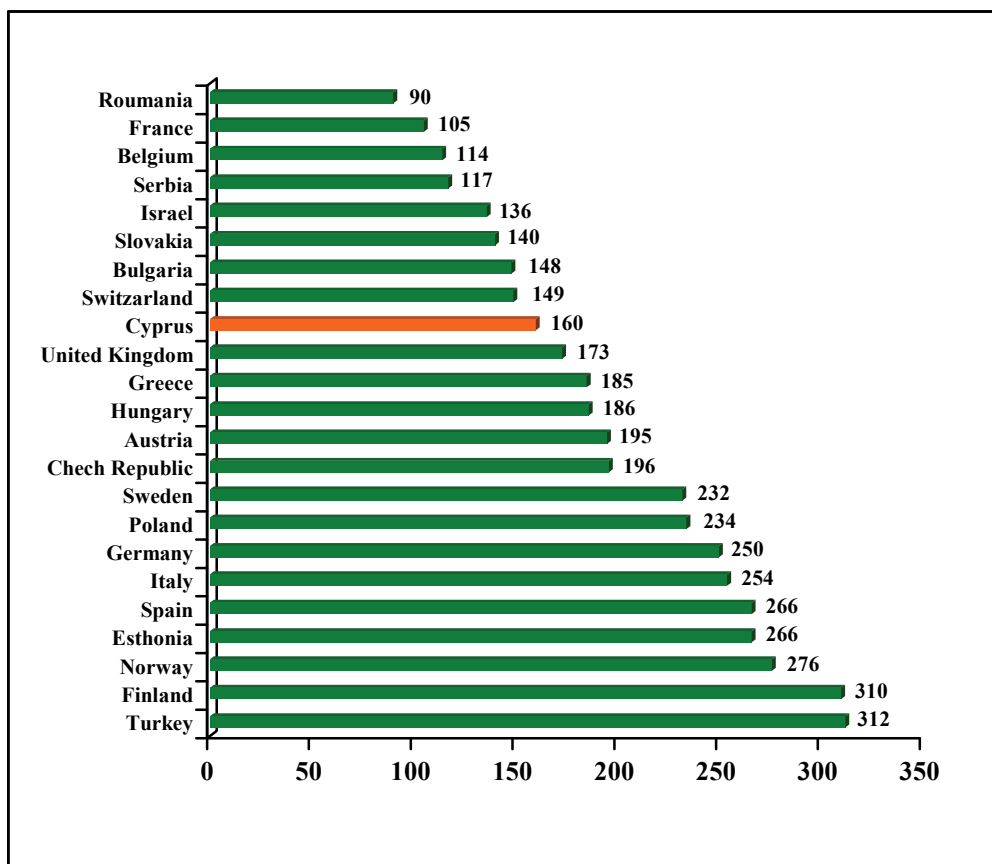


Figure 6. Annual incidence of Acute Coronary Syndromes per 100 000 habitants in Europe and in the neighbouring countries of Cyprus.

(Elements modified from Widimsky P et al. Eur Heart J 2010;31:943-957)

According to sex, the annual incidence of ACS was found significantly lower in women in comparison with men (41 ACS per 100 000 women contrary to 282 ACS per 100 000 men). The lower incidence of ACS in the female population may be attributed to the lower percentage of women with ACS who smoke (13.5% of women as opposed to 51.3% of men). In Greece, according to the GREECS study,⁶ the annual incidence of ACS in the male population was 340 ACS per 100 000 men and in the female population was 110 ACS per 100 000 women. In different regions of Great Britain⁴⁰ the annual incidence of ACS was 273-823 per 100 000 men and 66-256 per 100 000 women.

No difference was observed in the annual incidence of ACS between the habitants of the urban and rural regions of the Nicosia district.

Age of presentation of Acute Coronary Syndromes

The mean age of men with ACS was lower than that of women (men: 62.2±12 years old, women:70.2±12 years old, $P<0.01$). These findings are similar to the HELIOS study,⁷ where the mean age of men was 65±12 years old and of women 74±10 years old and also similar to GREECS study,⁶ where the mean age of men was 65±13 and of women 71±12 years. Regarding the age of patients, it was observed that for women most of ACS patients were presented with greater frequency 10 years later, compared to men and were increased with a rapid rate (Table 1,Diagram 1). For men the greater incidence of ACS was at the age of 50-59 years, while for women was at the age of 70-79 years. In an older study in Cyprus,¹¹ the greater incidence of ACS, was at the age of 61-70 years for men, while for women at the age of 71-80.

The mean number of admissions of patients with ACS in the Nicosia General Hospital was 1.1±2 patients daily. For all hospitals of the Nicosia district the mean number of admissions of patients with ACS was 1.6±1 patients daily. The relationship between men and women with ACS was 6.8 to 1. In an older study in Cyprus,¹¹ the relation of men to women with AMI was 5 to 1. In the GREECS⁶ and HELIOS⁷ studies the relation of men to women with ACS was 3 to 1. The difference in morbidity in coronary artery disease and in ACS between the two sexes is well known from many studies and the ratio of men to women is different in every country.^{3,18,19} Obviously this is attributed to the differences of socioeconomic conditions and the different prevalence of risk factors between the two sexes in different populations.^{3,20}

Seasonality

Studying the distribution of ACS during the year, a degree of seasonal distribution of admissions of patients with ACS was observed. More specifically, there were observed more admissions of ACS patients during the winter months in comparison with the summer months (Figure 4). More admissions of ACS patients were observed during January and December and less admissions in June and July (Figure 3). The same findings were observed in an older study of AMI amongst the Cypriot population¹¹ as well, and in the HELIOS⁷ study in Greece. In Italy, in a study of 64 191 cases of ACS it was observed that the ACS were more frequent during the winter months and less frequent during the summer months.²⁵ In resemblance to the present study, the ACS episodes in the Italian population were more frequent in January and less in July.

It is known that there is an increased incidence of ACS during the winter months and a lower incidence during the summer months,²² while as it is referred to in literature as well, the reduction of temperature by 1⁰C causes an increase of 5% in ACS admissions. The fact that the temperature drop is related to an increased risk for ACS, creates the suspicion that the cold weather may probably cause changes in blood pressure, blood lipids and blood in coagulation mechanisms. Positive association between the increase of relative humidity and the number of admissions for ACS has been identified from different studies.²² Other studies have shown an increased number of deaths (31%) from ACS during winter, in comparison with summer and particularly in the elderly patients.^{23,24} In the seasonal distribution of ACS the differences of dietary habits of patients during the winter and summer months probably contribute as well.

From the weekly distribution of the admissions of ACS (Figure 2), it was observed that the majority of admissions of ACS was on Monday (17.3%), after which follows a decline during the week until Sunday, in which fewer admissions (12.1%) were observed, ($P=0.029$ between Monday and Sunday and $P=0.04$ between Monday and Saturday). Similar results were observed in Greece, where in the HELIOS⁷ study more ACS episodes were observed on Mondays and less on Sundays, and in the Italian study as well, where ACS episodes were more often on Mondays and less often on Sundays.²⁵ This higher frequency of ACS on Mondays was attributed to the stress of returning back to work after the weekend break.²⁶

Predisposing factors

The most frequent risk factors observed were arterial hypertension and dyslipidemia in 49% of patients respectively, smoking in 48% and diabetes mellitus in 27.9% of the patients with ACS. A large percentage of the patients were obese (54.7%) and only 21.6% had normal body weight, according to the body mass index. The study also confirmed the great significance of the family history of early coronary artery disease, present in the 34.6 % of the patients, in both sexes. In the Greek study HELIOS,⁷ the prevalence of risk factors in the population of ACS patients was higher, mainly as far as arterial hypertension, obesity and smoking are concerned. Hypertension and obesity were observed in 59% and 73% of the Greek patients with ACS, compared to the 49% and 54.7% of the Cypriot patients with ACS. In the Greek population studied in the HELIOS⁷ study, the patients with ACS were smokers at a higher percentage (73%), in comparison to the Cypriot patients with ACS (48%). As far as Diabetes Mellitus and Dyslipidemia are concerned, there was no difference in the frequency of these factors between the patients with ACS in Cyprus and Greece.

The major predisposing factor for men was smoking (53.1%), while for women was arterial hypertension (67.3%). Compared to men, female patients with ACS had in a greater percentage hypertension (women: 67.3% as opposed to 46.3% of men, $P=0.005$) and passive smoking (women: 53.8% as opposed to 47.7% of men, $P=0.4$), while male patients with ACS were in a significantly greater percentage smokers, compared to women (men:51.3% in contrast to women:13.5%, $P<0.001$). These findings are similar to an older study of ACS in Cyprus,¹¹ in which it was observed that the most frequent predisposing factor in men was smoking (41.9%), while in women was hypertension (51.7%). Compared to that study, was observed that the percentage of men with ACS who were smokers, increased from 41.9% in 1990 to 51.1% in 2009 and the percentage of women with ACS who smoke increased from 3.5% to 13.5%, almost quadruple. From the same study, it was found that the percentage of women with hypertension increased from 51.7% to 67.3%, while the percentage of men more than doubled i.e. 21.6% to 46.3%.

In relation to the age of the patients with ACS, it seems that at the ages under 49 years old the main predisposing factors for ACS was smoking, family history of coronary artery disease and dyslipidemia. In the middle ages (50-69 years old), the main predisposing factors were smoking and dyslipidemia, while in the older ages, over 70 years old, the main

predisposing factor for ACS was hypertension. These observations lead to a more targeted treatment of risk factors by age and sex of the patients.

In male patients with STEMI, smoking history was more frequently present, where in women with STEMI passive smoking and hypertension were more frequently present.

In men with previous history of coronary artery disease, the most common form of expression of ACS was in the form of unstable angina, while in women was in the form of NSTEMI. In patients without previous history of coronary artery disease, ACS was usually manifested in the form of STEMI.

The nutritional habits and depression index showed no significant differences neither between men and women with ACS, nor between patients with STEMI, NSTEMI and unstable angina.

These findings emphasize the importance of early treatment of predisposing factors for the prevention of coronary heart disease, ongoing public information and targeted measures by the state, for a total ban of smoking, adoption of the Mediterranean diet, regular exercise, timely and effective treatment of dyslipidemia, diabetes and hypertension. The high percentage of patients with a family history of premature coronary heart disease emphasizes the importance of adoption by this group of patients, healthy dietary living and eating and regular medical surveillance for early treatment of first events of coronary heart disease.

Clinical manifestation and treatment of Acute Coronary Syndromes.

The type of ACS was based on the recent classification of the European Society of Cardiology²⁷ of ACS with persistent ST elevation (STEMI) and of ACS without persistent ST elevation (NSTE-ACS). The last group according to the presence or absence of troponin, separated afterwards in myocardial infarction without persistent ST elevation and unstable angina. In this study, the most common format for ACS was in the form of ACS without persistent ST elevation (NSTE-ACS:55%, STEMI:45% $p=0.003$). These findings are consistent with the findings of the literature and scientific data from recent surveys,^{2,3,28} which indicate that the ACS episodes are more common today in the form of NSTE-ACS, rather than in the form of STEMI. The relationship between STEMI and NSTE-ACS has changed over the years resulting in an increase of NSTE-ACS, with no clear explanation for this change. Possibly, this is due to the significant efforts for the prevention of coronary heart disease over the past 20 years. Unlike the

GREECS⁶ study, where it was observed that women with ACS were more likely to be admitted with the picture of unstable angina and men with a picture of STEMI, this study showed no difference in the type of ACS between men and women with ACS.

Based on the guidelines of the European Society of Cardiology,¹⁵ patients with ACS and persistent ST elevation should be treated within 6 hours since the onset of pain with medical or mechanical reperfusion. Of the total number of the patients admitted with ACS, 33.6% underwent medical reperfusion treatment with tenecteplase-TNK-t PA. In particular 74.4% of STEMI patients were treated with medical reperfusion and 1.6% were treated with mechanical reperfusion. Rescue angioplasty was necessary for 13.7% of patients with STEMI.

Treatment of patients with STEMI varies in European countries.¹⁰ These differences are most pronounced among the countries of Northern, Central and Western Europe, where mainly mechanical reperfusion therapy (primary angioplasty) is performed in 60-90% of STEMI patients and countries of Southern Europe and the Balkans, where the treatment with medical reperfusion (thrombolysis) still dominates.¹⁰ A study of the reperfusion treatment of STEMI in 30 European countries,¹⁰ showed that the overall reperfusion therapy (thrombolysis or primary angioplasty) was given to the 37-92% of patients, according to the European country. Indicatively, with medical reperfusion, 55% of patients with STEMI were treated in UK, 45% in Romania, 44% in Portugal, 40% in Finland, 31% in Belgium, 35% in Austria, 28% in France and 7% in Germany¹⁰ (Figure 7). According to the same study, in the neighboring countries of Cyprus, pharmaceutical reperfusion was applied to 41% of patients with STEMI in Greece, to 29% of patients in Turkey and to 16% of patients with STEMI in Israel. Mechanical reperfusion was applied to 92% of STEMI in the Czech Republic, to 81% in Germany and Switzerland, to 72% in Poland, to 70% in Croatia, to 66% in Sweden and to 64% of patients with STEMI in Hungary (Figure 7).

In Great Britain,^{10,28,29} 55% of patients with ACS were treated with thrombolysis and 24% of patients with primary PCI. In Germany^{10,30} 81% of patents were treated with primary PCI, 7% with thrombolysis and 12% without reperfusion therapy. In France 33% of ACS were treated with primary angioplasty, 28% with thrombolysis and 39% without reperfusion therapy.

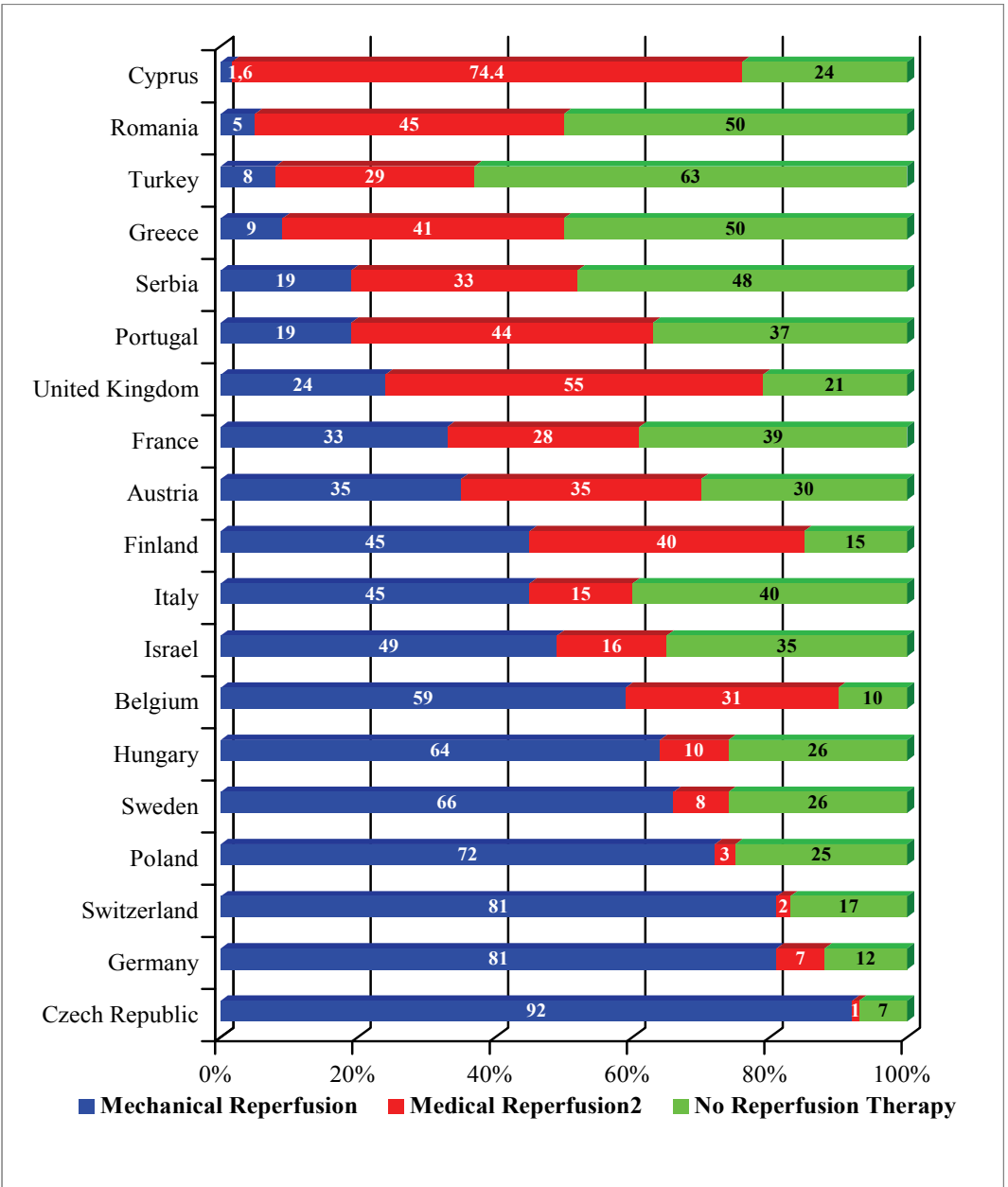


Figure 7. Treatment of patients with acute coronary syndrome with persistent ST elevation (STEMI) in Europe and neighbouring countries of Cyprus. (Data modified from Widimsky P et al Eur Heart J 2010; 31:943-957)

In the neighboring countries of Cyprus, Greek study HELIOS⁷ showed that approximately 41% of patients with STEMI were treated with thrombolysis, 9% with primary angioplasty and 50% did not receive any reperfusion therapy. In Turkey, according to TUMAR Registry¹⁰ similar results were observed, where only 29% of ACS received medical reperfusion therapy, 8% were treated with primary angioplasty and 63% did not receive any reperfusion therapy. In Israel, on the basis of ASCIS Registry,¹⁰ 49% of patients with STEMI were treated with primary PCI, 16% with thrombolysis and 35% with no reperfusion therapy.

The present study shows that the percentage of patients with STEMI in Cyprus treated with reperfusion therapy (pharmacological or mechanical), is among the highest in Europe (76%), Figure 7. The greater percentage of patients with ACS in Cyprus is treated with pharmacological reperfusion (74.4%). This percentage has increased significantly since 1996, when only 45.2% of patients with acute myocardial infarction were treated with pharmacological reperfusion.³² Pharmacological reperfusion is a satisfactory alternative therapy to reperfusion in patients with STEMI, especially for hospitals without catheterization laboratory equipped with experienced staff.

The beneficial effects of thrombolysis are widely known in patients undergoing treatment on time. A meta-analysis of 22 studies³³ showed that thrombolysis when applied on less than 120 minutes since onset of symptoms is accompanied by a greater reduction in mortality. In the CAPTIM³⁴ study that compared patients with STEMI treated with mechanical reperfusion (primary PCI) or pharmacological reperfusion (thrombolysis), which was implemented early in the ambulance that transported the patient to the hospital, showed that: (a) patients who were thrombolysed in less than two hours since the onset of pain had a better prognosis in a five-year survival compared with patients treated with primary PCI (5.8% as opposed to 11.1%, $P=0.04$). (b) patients treated after two hours since the symptom's onset, had the same five-year survival, whether treated with pharmacological or with mechanical reperfusion (14.5% as opposed to 14.4% $P=0.91$).

The number of patients with STEMI treated during 2009 with primary angioplasty was low (1.6%). Rescue angioplasty after the initial treatment with thrombolysis was required in 13.7% of STEMI patients. Nicosia General Hospital is equipped with two cardiac catheterization laboratories and experienced medical and paramedical staff. A similar structure exists in the Limassol General Hospital which covers the districts of Limassol and

Paphos. There are also private hospitals in Nicosia and Limassol with hemodynamic catheterization laboratories. Overall in Cyprus, which has 800 000 inhabitants, there are five cardiac catheterization laboratories, three in Nicosia and two in Limassol. Based on these data it is possible to treat the ACS-STEMI patients in Cyprus along with the choice of mechanical reperfusion with primary angioplasty. The beneficial effects of this treatment is well known compared with medical reperfusion, provided that it is implemented in accordance with the directives of the European Society of Cardiology,²⁶ within the first two hours of the symptom onset. According to a recent study of reperfusion therapy for patients with STEMI in thirty European countries,¹⁰ it was found that hospital mortality was lower in patients treated with primary angioplasty (2.7% -8%) compared to patients treated with thrombolysis (3.5% -14 %).

A study of 1100 patients with acute myocardial infarction hospitalized in Nicosia General Hospital,³² from 1989 to 1993, showed that 45% of patients with acute myocardial infarction arrived at the hospital in time less than 60 minutes and 67% in time less than 120 minutes since the onset of symptoms. The early arrival of patients with acute myocardial infarction was attributed to the small geographical area of Cyprus, the short distances between place of residence of the patients and the hospital, and the continuous updating of patients for the prevention and treatment of heart disease. Regarding these data we believe that in Cyprus all preconditions exist for management of patients with STEMI with primary PCI. The implementation of a program treating STEMI patients with primary PCI, other than the known beneficial effects on prognosis and survival of the patients,¹⁰ will allow for a faster release of hospital beds and will offer significant economic advantages by reducing hospitalization time of the patients.

Coronary angiography was submitted to the 69.1% of patients with ACS (72.8% of men and 44.2% of women, $P < 0.05$). No significant difference was observed in performance of coronary angiography between the various forms of ACS. 68.9% of patients with STEMI, 72.2% of the patients with NSTEMI and 70.9% of patients with unstable angina underwent coronary angiography.

Studying treatment options for patients with ACS, after the performance of the coronary angiography, it was found that most of the patients were treated in the same session with angioplasty and only 11% were referred for CABG. This rate differed between men and women where, for the male

patients with ACS who underwent coronary angiography 43.3% were treated with angioplasty and 10.4% with CABG. For women who underwent coronary angiography 17.3% were treated with angioplasty, while the percentage of women who underwent CABG was higher than that of men (women: 15.4%, men:10.4%, $P=0.33$). The differences in the treatment of ACS between the two sexes have been demonstrated in several European academic records (Registries).^{35,36} In contrast to men, women are driven less often in diagnostic tests, coronary angiography and myocardial revascularization procedures. The special anatomical features, such as the small size of coronary arteries, make it more difficult to treat stenosis in women and affect the use of intracoronary stent.

The in-hospital mortality of patients with ACS was quite low (3.5%). The mortality rate showed significant decrease compared to Cypriot data from 1992,^{11,12} where the mortality was 8.7% and is considerably lower than the mortality referred in studies from other countries. In Greece and specifically according to the HELIOS⁷ study, the in hospital mortality was 7.7%, while in other European countries¹⁰ it ranged from 5% - 14%. Based on the above data, it is shown that the in-hospital mortality rate of patients with ACS in Cyprus may be the lowest in Europe (Figure 8). This is probably due to the peculiarity of Cyprus, where as mentioned above, the short distances between place of residence and hospital, the good road network and raising awareness of patients about heart attacks, result in transporting patients with ACS promptly to the hospital and treating them with reperfusion in a short period of time. This observation confirms once again that one of the most important factors in the outcome of patients after an ACS, is the rapid transfer to the hospital and the timely application of reperfusion therapy (pharmacological or mechanical).

Medical treatment at discharge

It is well known and documented,¹⁵ that some interventions can improve prognosis after an ACS. The recommended medication that relates to increased life expectancy after an ACS, includes aspirin, beta-blockers, angiotensin converting enzyme inhibitors and angiotensin receptor antagonists, statins, etc. Discharge treatment in patients with ACS, including the above medications, is considered as a qualitative indicator of inpatient treatment and good patient care after discharge.

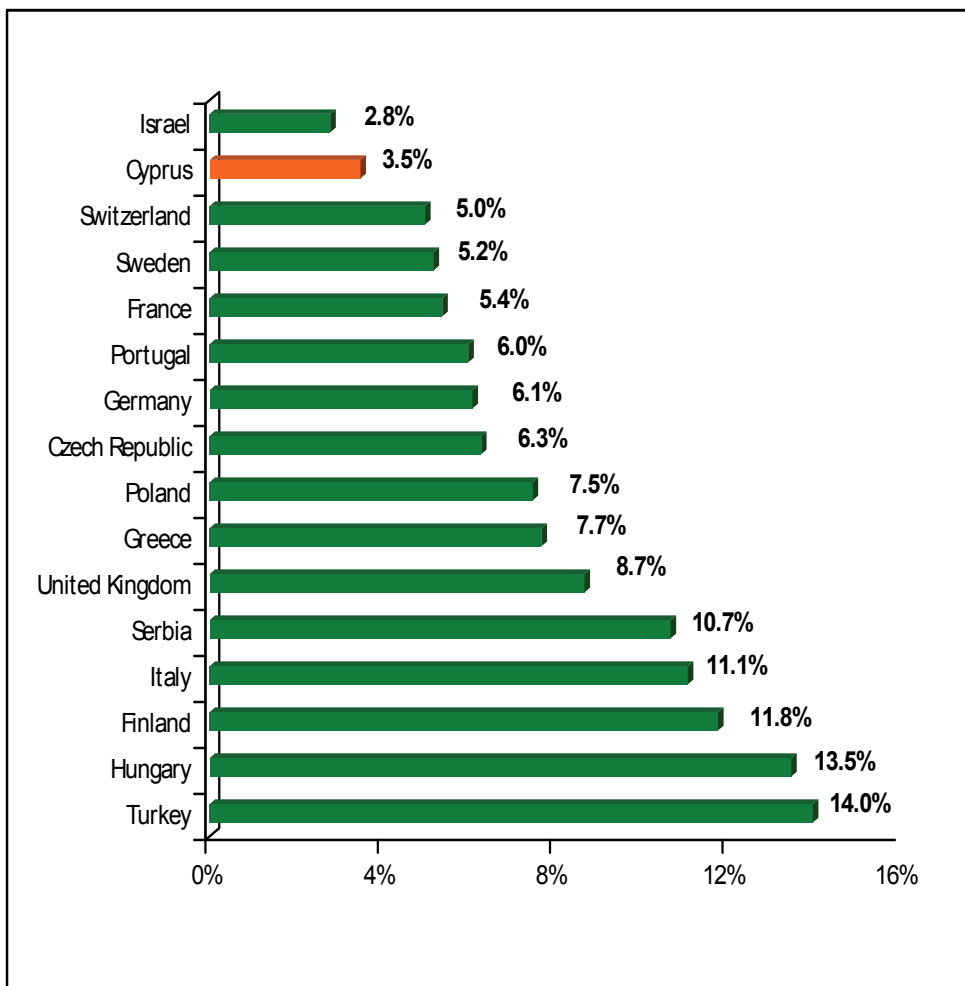


Figure 8. In-hospital mortality of patients with Acute Coronary Syndrome in Europe and neighbouring countries of Cyprus.

(Data modified from Widimsky T. et al. Eur Heart J 2010; 31: 943-957)

The treatment of patients on discharge after the initial hospitalization with ACS included prescribing aspirin in 78.4% of cases, statins in 74%, beta receptor blockers in 68.2%, clopidogrel in 64.2% and ACE inhibitors or angiotensin receptor antagonists in 57.1% of patients with ACS. Although there was a higher percentage of men receiving angiotensin receptor blockers and calcium antagonists compared with women and more women

were taking nitrates compared to men, but with the exception of nitrates, no statistically significant differences were observed in the prescription of these drugs among gender.

According to the Euroaspire III study,³⁸ the percentage of patients in Cyprus, receiving statins after an ACS was among the highest in Europe (Cyprus: 91.2% vs. 79.8%, which was the average in Europe). Statins prescription at discharge was included in 74% of patients with ACS. This percentage was higher than that of a European registry study on ACS,² where only 50% of patients were receiving statins, but relatively lower than the proportion of patients in the HELIOS⁷ study, where percentage of patients to whom statins was prescribed at discharge was 82%.

Beta-receptor blockers were administered to 68.2% of the patients in this study, slightly lower than the percentage of the HELIOS⁷ and GRACE³⁶ studies where the rate for beta-blockers after an ACS was 79% and 74.2% respectively. Similarly, the proportion of patients receiving aspirin in the discharge prescription was slightly lower (78.4%) of the corresponding rate of the patients in the HELIOS⁷ study (88%) and the GRACE³⁶ study (88.7%).

The percentage of patients treated with angiotensin converting enzyme inhibitors or angiotensin receptor blockers was 57.1%, lower than the proportion of the GRACE³⁶ and HELIOS⁷ studies, where the above mentioned medicines were administered to 69.8% and 75% of patients respectively.

Studying the discharge treatment of patients hospitalized with ACS in Cyprus was found to be comparable of the treatment followed in other European countries and in accordance with the official recommendations and guidelines of the European Society of Cardiology.¹⁵

Characteristics of the lifestyle of patients with ACS

In the present study, it was attempted to explore some features of the lifestyle of patients with ACS. The beneficial effect of the Mediterranean diet on primary and secondary prevention of coronary heart disease is well known. The degree of patient adaptation to Mediterranean diet, as was measured by a diet score, showed with a small percentage but not with a significant difference, that men follow a more Mediterranean-style diet compared to women. In contrast to the GREECS⁶ study, where it was observed that patients with unstable angina tended to follow a more

Mediterranean-style diet in comparison to patients with STEMI, no difference was found in the diet score between the different types of ACS in this study.

In GREECS study,⁶ it was observed that patients with no physical activity were more likely to suffer from STEMI than NSTEMI and unstable angina. In the present study the above findings were not found, but it was observed, without statistically significant difference, that men with heavy physical activity were more likely to suffer from unstable angina than STEMI and women were more likely to suffer from NSTEMI than STEMI ($P = NS$).

No significant difference was observed in the rate of depression among men and women with ACS, as well as between the different forms of expression of ACS. In the GREECS⁶ study, the depression score was higher in patients with STEMI, compared to patients with unstable angina.

Regarding the education level, no significant relationship was observed between education level and type of ACS, although it was observed, without statistically significant results, that patients with primary education were more likely to experience unstable angina than STEMI, ($P = NS$).

From the study of the marital status of patients, a higher percentage of ACS in married men was observed, compared to married women (married men: 84.1% versus 42.9% of married women $P < 0.001$) and widows (49%) than widowers (5.8%) $P < 0.001$. These findings could be due to the fact that the average age of women at the timing of the ACS was by a decade greater than that of men, where the large majority of men were married at the time of the incident, while the majority of women were widows. The assessment of marital status showed no significant relationship between marital status and type of ACS. With no statistically significant differences, widowed male patients with ACS were more likely to experience unstable angina, rather than STEMI and NSTEMI ($P = NS$) and unmarried and widowed women with ACS were more likely to experience STEMI than other types of ACS ($P = NS$).

CONCLUSIONS

We conclude that the treatment of ACS in Cyprus is similar to the treatment of ACS in southern Europe and in most neighboring countries of Cyprus. The greater percentage of patients with STEMI (74.4%) is treated during the in-hospital period with reperfusion therapy, mainly pharmacological. The

high percentage of patients with ACS submitted to reperfusion therapy in combination with the early arrival of patients to the hospital due to the small distances in Cyprus, has led to a very low mortality rate (3.5%), perhaps the lowest in Europe.

For the same reasons there are all the preconditions for the application of primary PCI of all STEMI patients in Cyprus, which is applied predominantly in northern European countries. The simultaneous adoption of this treatment will contribute to an even better treatment of patients with ACS in Cyprus and eventually reduction of time and cost of hospitalization of patients.

The study showed that the majority of patients after an ACS follow the appropriate medication, as determined by the guidelines.

The largest percentage of men were presenting ACS at the age of 50-59 years, while more women at the age of 70-79 years.

The largest percentage of ACS occurs during the winter months of the year, mainly in January and December and the early days compared to the last days of the week. This observation will help in the better management of hospital beds and better planning of non-emergency admissions and cardiac diagnostic tests in the hospital, which can be scheduled in the months and days when there are fewer emergency admissions with ACS in the hospital according to the data of the study.

The main predisposing factors for ACS, seem to differ according to gender and age of the patients. So it seems that men's main predisposing factor for development of ACS is smoking, while in women is hypertension. In relation to the age of patients with ACS it seems that at ages below 49 years the main predisposing factors for ACS is smoking, family history of coronary artery disease and hypercholesterolemia, in the middle ages, i.e. 50-69 years, is smoking and hypercholesterolemia, while in older ages, i.e. over 70 years, is mainly arterial hypertension. It was also observed that 78.4% of patients with ACS were overweight. These observations will lead to a more targeted treatment of risk factors by age and sex of patients.

In male patients with previous history of coronary artery disease the most common form of expression of ACS was in the form of unstable angina and

in women in the form of NSTEMI. In patients without previous history of coronary artery disease, ACS was presented predominantly as STEMI.

The incidence of ACS in the Cypriot population was set at 160 ACS per 100 000 inhabitants (41 ACS per 100 000 women and 282 ACS per 100 000 men). Roughly, this means that in Cyprus three (3) ACS episodes occur per 1000 men and four (4) ACS episodes per 10 000 women. On this basis, it is estimated that every year 1342 patients are admitted to Cypriot hospitals with an ACS. There was no difference in annual incidence of ACS between the inhabitants residing in urban and rural areas.

In comparison with the countries of Europe, the annual incidence of ACS in Cyprus is in about the average of European countries, with higher annual incidence of ACS in Finland (310 per 100 000 inhabitants) and a lower annual incidence in Romania (90 per 100 000 inhabitants). For neighboring countries of Cyprus, with the exception of Israel (136 patients per 100 000 inhabitants), the annual incidence of ACS in the Cypriot population is relatively less than the incidence of ACS in these countries (Greece: 185 per 100 000 inhabitants, Turkey: 312 per 100 000 inhabitants).

The relatively lower incidence of ACS in Cyprus probably is contributed to the public campaigns to prevent cardiovascular diseases and the possible gradual change in lifestyle and dietary habits of Cypriots. However, high rates of patients with ACS who are obese, not exercised, are smokers, have high cholesterol and hypertension should lead to targeted strategies systematically addressing the Cypriot population's interest to these factors. These factors with a systematic application of information and prevention programs that begin from childhood, it is certain that will lead to a significant reduction of the factors that predispose to the development of coronary heart disease and by extension to the ACS in the Cypriot population.

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