"Ovidius" University

Doctoral School of the Faculty of Medicine

DOCTORAL THESIS ABSTRACT

Epidemiological considerations, therapeutic and evolutive

prognosis in acute coronary syndromes

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Constanţa

2012

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ACS- acute coronary syndromes

NCD - noncommunicable diseases

MI- myocardial infarction

RoStemi- Romanian Registry for the Stelevation myocardial infarction

URL- upper reference limit

HTA-arterial hypertension

INTRODUCTION

According to the National Institute of Public Health of the Ministry of Health of Romania, deaths by cause in 2011 maintain the feature from recent years, most deaths being caused by diseases of the circulatory system **(151,538).**

It is estimated that the cardiovascular mortality will increase from 17 million in 2008 to 30 milion in 2030. Of all NCD highest proportion is occupied by cardiovascular disease by 48%, followed by cancers by 21% and respiratory diseases by 12%. Diabetes is responsible for 3.5% of all deaths due to noncommunicable diseases.

One of the most serious cardiovascular disease is myocardial infarction. The overall incidence in acute myocardial infarction in 2008 was 5.1 cases per 100 000 inhabitants. Over 25 percent of cardiovascular deaths are due to myocardial infarction.

This paper is inspiered from RoStemi database model that summarizes the data obtained from patients with myocardial infarction registered in the first Romanian Registry for acute myocardial infarction with ST-segment elevation (Romanian Registry for the Stelevation myocardial infarction, RO-STEMI).

The particularity of the work of this research relates to the diversification of cases of acute myocardial infarction with ST-

segment elevation by deepening a possible new criterion / risk factors: ethnicity.

In this study, data were collected from hospitalized patients between 2008 - 2011 within the Cardiology Clinic I of Constanta County Emergency Hospital.

In total, data were analyzed for a total of 1320 patients. Of these, 1139 people have been defined as the general population and 181 Turkish-Tatars.

We have studied Turkish Tatar population due to their specific ethnic substantially different from those of the general population and because now, according to data from NIS (census 2002) Turkish-Tatar population totals 56,033 people of which 47,476 live in Constanta (84 , 72%).

Also it should be noted that the percentage is the Turkish-Tatar population in total population Constanta County (715,151), namely 6.63%.

This paper aims to highlight some particular installation / development of myocardial infarction ST segment elevation compared to patients from the two groups in the study: general population and the Turkish-Tatar population.

This study was conducted in the Cardiology Clinic I of Constanta County Emergency Hospital, under the careful and meticulous guidance of Mrs. Univ. Dr. Craigslist Elvira.

Especially thank Prof. Univ. Dr. Craiu Elvira, MD Chief of Cardiology Clinic I of Constanta County Emergency Hospital,

I.Acute myocardial infarction with ST-segment elevation

I.1 Definition

Morfopatolagic diagnosis of myocardial infarction is defined by cell death - of myocytes - due to prolonged ischemia. Cell death is characterized pathologically by bands coagulation necrosis and / or contraction which usually evolves through oncosis, but may results in a lesser degree and apoptosis [1]. Also, myocardial infarction can be defined in terms of clinical, electrocardiographic and biochemical. These criteria correspond to the universal definition of myocardial infarction published in 2007 [2].

I.1.1 Criteria for acute myocardial infarction.

The term myocardial infarction should be used when there is evidence of myocardial necrosis in a clinical context consistent with myocardial ischemia. Based on these circumstances, any of the

following criteria are consistent with the diagnosis of myocardial infarction:

1. Detection increase/decrease of necrosis infarction markers (Preferably troponin) with at least no higher than the 99th percentile of the upper reference limit certificate of myocardial ischemia by at least one of the following elements:

   - symptoms of ischemia;
   - changes of the ST segments suggestive of ischemia
   - ST segment elevation from J point in at least two adjacent drift ≥ 0.2 mV in V2-V3 and ≥ 0.1 mV in other drifts or recent left bundle branch block;
   - the appearance of new pathological Q waves on ECG;
   - echocardiographic evidence of turbulent myocardial kinetics.

2. Cardiac sudden death by cardiac arrest, often with symptoms suggestive of myocardial ischemia along with ST segment elevation supposedly new or branch block and / or evidence of fresh thrombus by coronary angiography and / or autopsy; death occurred before bood samples could be harvested or at an earlier time than cardiac biomarkers manifested.

3. In percutaneous coronary intervention in patients with basal normal troponin T values, increase of cardiac biomarkers over the 99th percentile of URL are indicative of periprocedural myocardial necrosis. By convention, increases of biomarkers greater than 99th percentile 3x URL have been designated as defining periprocedural myocardial infarction; a subtype of thrombosis stent related is also recognized.

4. Regarding aortocoronarian bypass, in patients with basal T and normal troponin, increases of cardiac biomarkers over the 99 - percentile of URL are indicative of periprocedural myocardial necrosis. By convention, increase of more than 5x 99th percentile URL biomarkers, adding pathological Q waves or new bundle branch block and a new occlusion angiography documented of a coronary graft or a native or imaging evidence of new loss of viable myocardium have been designated as defining for peri-bypass infarction.

5. Morphological evidence of acute myocardial infarction.

II. Epidemiology

According to the latest Statistical Yearbook published by the WHO, non-communicable diseases were responsible for 37 (63%) of the total of 57 million deaths worldwide in 2008.

It is estimated that the nature cardiovascular mortality will increase from 17 million in 2008 to 30,000,000 in 2030. Of all NCD highest proportion is occupied by cardiovascular disease by 48%, followed by cancers by 21% and respiratory diseases by 12%. Diabetes is responsible for 3.5% of all deaths due to noncommunicable diseases.

1.   IMA epidemiology in Romania

According to data reported by the Ministry of Health of Romania overall deaths and 2011 cases are characteristic of recent years, **most deaths by diseases of the circulatory system (151,538) and** tumors (48 356), followed by diseases of the digestive (14499) respiratory diseases (12,460), and injuries and poisonings (10,534). [4]

2.   IMA Epiemiology across EUROPE

At European level, mortality due to CVD peaked in the early '60s, but since then began to decrease in intensity, it has been well established in the past 2 decades. In EU 15 (the 15 countries of the European Community by 2004: Austria, Belgium, Denmark, Germany, Greece, Finland, France, Ireland, Italy, Luxembourg, Portugal, Spain, Sweden, the Netherlands and the UK) CVD mortality declined from 1975 to 1995 by 40%.

III. RO-STEMI DATABASE

ROSTEMI database summarizes data obtained in patients with myocardial infarction registered in the first Romanian Registry for acute myocardial infarction with ST-segment elevation (Romanian Registry for the Stelevation myocardial infarction, RO-STEMI).

RO-STEMI appeared in 1997 by uniting the efforts of three centers (Emergency Hospital "Floreasca" Bucharest, Municipal Hospital Roman, Braila County Emergency Hospital).

Through the sheer volume of information from centers spread throughout the country, the registry has become progressively a reflection of parts specific features of demographic, therapeutic and progressive that STEMI patients admitted to hospitals in recent Quarter I of Romania. [1]

IV. Turkish-Tatar population in Constanta

Constanta county share of romanians is higher than the national average of 89.5%. Constanţa also focuses 98% of the Tatar population and 81% of the Turkish population. Instead, here is a rate lower than the national average of Hungarians, Germans and Roms.

Currently, according to data from NIS (census 2002) Turkish-Tatar population totals 56,033 people of which 47,476 live in Constanta (84.72%).

Also it should be noted that the percentage is the Turkish-Tatar population in total population Constanta County (715,151), namely 6.63%.

Population structure of DOBROGEA by nationality and districts

Dynamic characteristics of ethnic migration Dobrogea was maintained after 1996, as evidenced by the 2002 census.
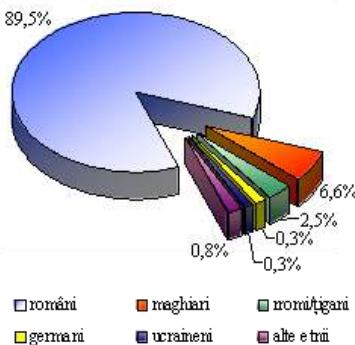
Figure V.1 Structure of Romania's population after the 2002 Census

IV. MATERIAL AND METHOD

In this study, data were collected from hospitalized patients in 2008 - 2011 at the Cardiology Clinic I of the Constanta County Emergency Hospital.

Data from case report forms were introduced in an electronic model. This model contains information about certain characteristics of the patient population of interest, namely age, gender and ethnicity. Depending on ethnicity, patients were randomized into two groups: patients of Turkish-Tartar origin, and patients of other ethnicities (Romanian ethnic majority), hereinafter referred to as general population.

To analyze the information gathered they were grouped, as appropriate, depending on:

- their year in which they were recorded (2008,2009,2010 and 2011),
- according to age group (<45 years, 45-59 years, 60-75 years, > 75 years)

In total, data were analyzed for a total of 1320 patients. Of these, 1139 people have been defined as the general population and 181 Turkish-Tatars. The following table is centralized data on the number of patients in the two groups subjected to statistical analysis

Table VI.1 Patient distribution by lot

	In 2008	In 2009	In 2010	2,011	Total
Total cases	418	176	307	419	1,320
General population	362	152	273	352	1,139
Turkish Tatar population	56	24	34	67	181

Criteria for inclusion in the risk categories were represented by:

- Arterial hypertension - were considered risk factors people with blood pressure values above 140/90 mmHg (according to the European Guidelines for Hypertension, 2007).
- Smoking - represents certainly a major risk factor for occurrence of acute coronary syndrome (presenting the risk of two times to present their STEMI in comparison with non-smoking patients) [1] is one of the main causes of premature cardiac death that can be prevented by changing behavior. Studies highlight that once ceasing smoking significantly reduces the risk of death compared with those who continued to habit. [2]
- Dyslipidemia was evaluated based on LDL cholesterol, the critical value being considered the one recommended by The European guide for management of ST elevation MI (2007), or <100 mg / dl. [3]
- Diabetes, another major risk factor for cardiovascular diseases is also evaluated. Evaluation was based on analyzes of history and during the internal evaluation , where a value> 126 mg / dl [4]
- Obesity - was based on evaluting mass index body. According to WHO recommendations we

considered obese people with a BMI greater than 30 kg / m ^{2}

- Old myocardial infarction - presence of an event in their history, assessed by history.

Information about treatment performed included data on the type of treatment (conventional thrombolysis or angioplasty), various protocols followed, the type of medication administered. Since Constanta County Emergency Hospital has not performed angioplasty, patients were transferred to other specialized services with indication of angioplasty and are considered to have benefited from this treatment, they are also excluded from the analysis of the evolution after admission**.**

VI RESULTS

For a better analysis of the data, we divided the patients into four age groups (<45 years, 45-59 years, 60-75 years and> 75 years) and analyzed the differences that occur between men in the general population and Turkish - Tatars.

Patient distribution by age is illustrated below. It is noted that the largest number of patients belonging to the age group 60-75 years (37.05%). Follow in order those aged between 45-59 years (30%) and those older than 75 years (26.29%).Approximately 7% of patients were aged less than 45 years.
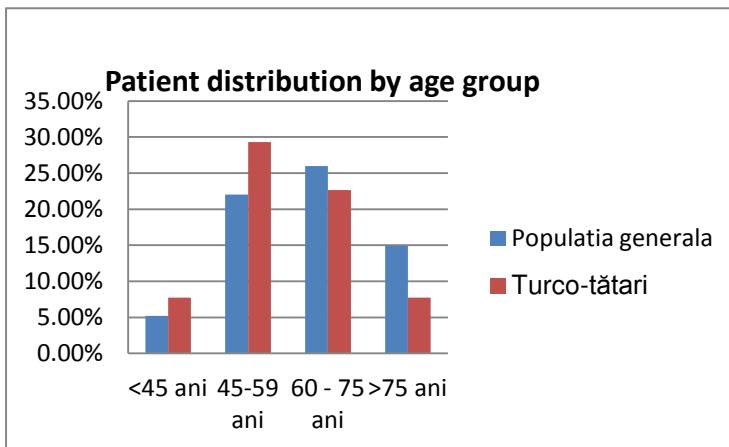
Figure VII.4 Patient distribution by age group

Chi-square test is statistically significant, thus showing that the distribution of patients according to age significantly differ between the two populations studied.

When analyzing the percentage distribution is noted that if the Turkish Tatar population percentage of patients younger than 45 years is 9.94%, compared with the general population, where for the same category the percentage of 6.15%. For the period 45-59 years there is a difference of almost 10 percent between Turkish-Tatar ethnic patients and the general population (38.12% vs 28.71%). This difference is statistically significant at a level p <0.05.

Below is plotted the percentage distribution of men according to age group and category to which they belong (or Turkish-Tatar general population). It is noted that the percentage of ethnic Turkish-Tatar men younger than 60 years represent almost 55% of men in this ethnic group.

Age pyramid for men

|	Turco-tătari	Populatia generala
>75 ani	11.48%	21.91%
60 - 75 ani	33.61%	38.14%
45-59 ani	43.44%	32.35%
<45 ani	11.48%	7.60%

Procente
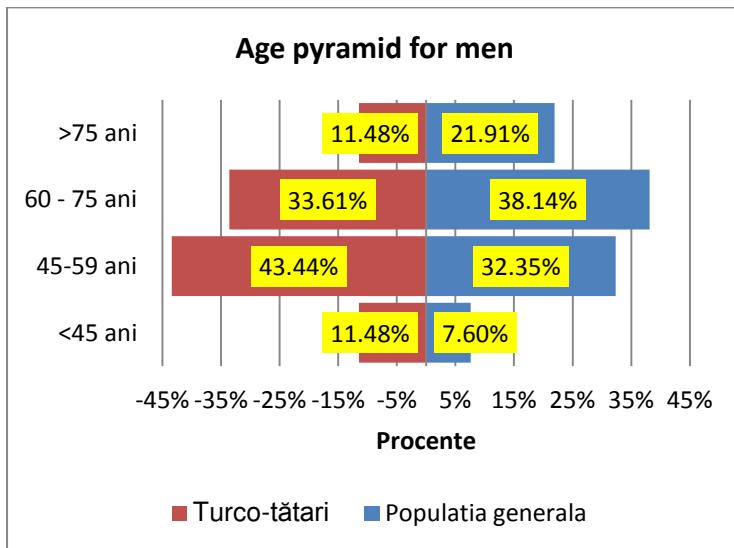
Figure VII.5 age pyramid for men

For age groups <45 years and 45-60 years group noted that the percentage of Turkish-Tatar men is higher than the percentage of the general population. The results indicate that differences are statistically significant for age groups 45-59 years (where Turkish-

Tatar percentage is 43.44% compared to that of men in the general population is 32.35%) and age group> 75 years (11.48% or 21.91% Turko-Tatars general population) at a level of statistical significance p <0.05.

IV.1 Circadian distribution of onset of pain

It is noted that most events were held for the general population between 8:00 to 11:59, while the population of the Turkish-Tatar origin with most events range was 4:00 to 7:59, followed closely the range 8:00 to 11:59.
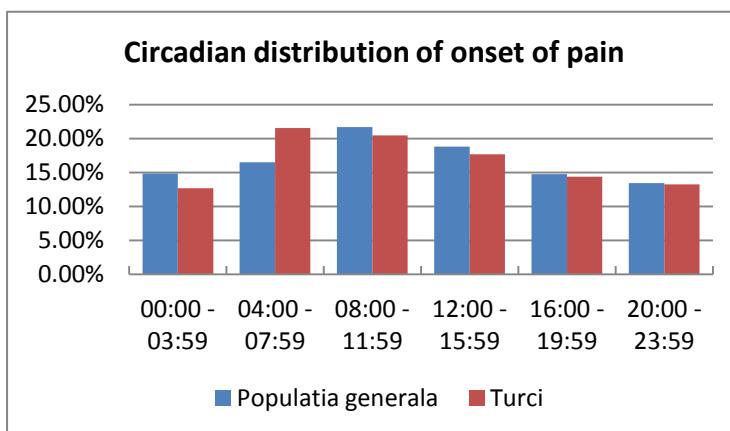

Figure VII.10 Circadian distribution of onset of pain

Observed distribution pattern observed respects international literature regarding circadian distribution of the occurrence of cardiovascular events.

According to the results obtained from the Chi-square test can not be said that there is a statistically significant difference in the distribution circadian onset of pain among the general population and the population of Turkish-Tatar origin. (P = 0.695).

IV.2 Distribution function interval from the onset of chest pain and until admission

For the general population, the highest proportion of patients, 34.33% were shown in 0-3 hours time. Regarding the Turkish-Tatar ethnic population is observed that most were admited during the time between 3 and 6 hours (29.28%).

Chi-square calculated value is 32.753. This value for 10 degrees of freedom corresponds to a p-value <0.001. It can be seen therefore that there is a statistically significant association between ethnicity powerful people and the interval between onset of pain and delay in admission.

IV.3 Analysis of Cardiovascular Risk Factors
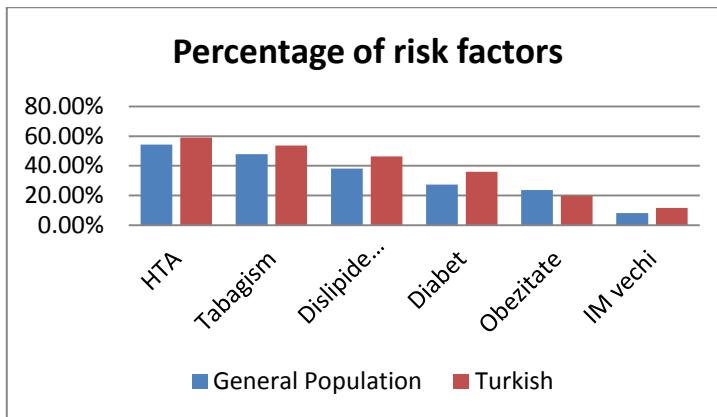
Figure VII.23 Percentage of risk factors

The most common risk factor is the high blood pressure, a condition present in approximately 55% of patients in the general population and over 59% of patients in the Turkish-Tatar population. Follows in descending order of prevalence of smoking (47.76% and 53.59%), dyslipidemia (38.19% and 46.41%), diabetes, obesity and old myocardial infarction. It is noted that in all cases, except for obesity, these risk factors are present in a higher percentage in the Turkish-Tatar population.

IV.3.1 Old myocardial infarction

Within all patients evaluated in this study, 8.17% of the general population and 11.60% of the Turkish-Tatar had at least one prior myocardial infarction.
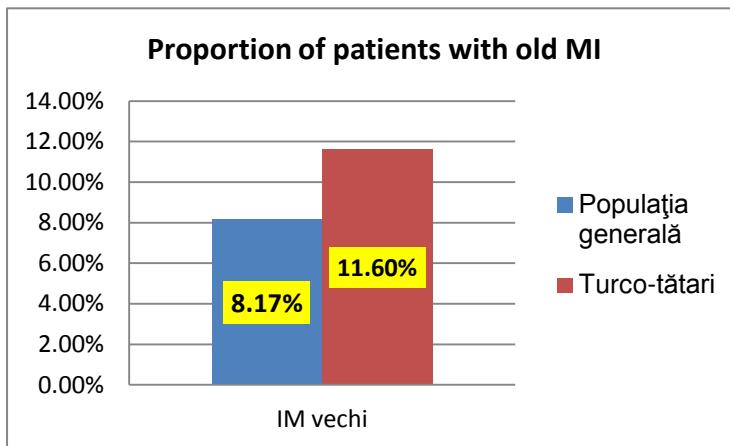
Figure VII.39 Proportion of patients with old MI

Odds ratio (odds ratio), an index that calculates the chances of an event to take place within a group versus another group, in this case has the value 1.47 (95% CI 0.893 to 2.438). The result is not statistically significant, p = 0.128. It is therefore apparent that there is no link regarding history of MI and ethnic group originating patients.

In the period 2008 - 2011 in the general population is a slight downward trend in the percentage of patients with old myocardial infarction, the percentage decreased steadily from 9.1%

in 2008 to 7.4% in 2011. Turkish-Tatar population in there is a tendency to maintain a constant proportion of patients with old myocardial infarction.

Old MI Developments during 2008 to 2011
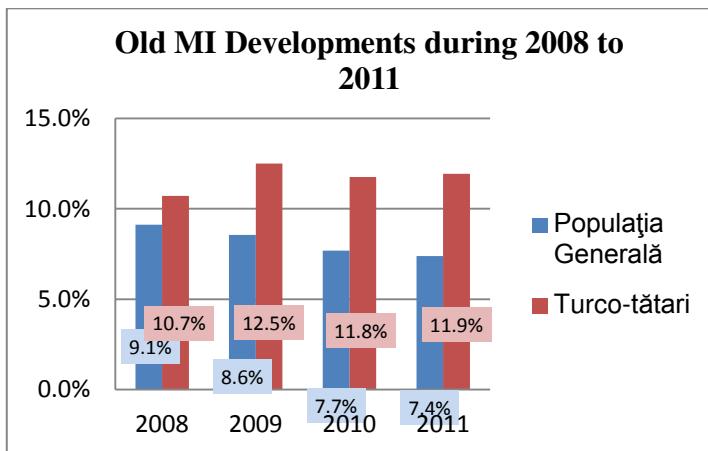
Figure VII.40 Old MI Developments during 2008 to 2011

Depending on the age group in the general population there is a maximum prevalence in people aged 60 to 75 years (12.5% of them showing a old myocardial infarction). Conversely, in the Turkish-Tartar population the highest percentage of patients with a history of myocardial infarction is recorded in patients older than 75 years.

IV. Treatment

Treatment progress over the four years of the study showed a slight increase in the percentage of patients who received interventional treatment (angioplasty). Regarding conventional and

thrombolytic therapy is noted that these overall it keeps to a relatively constant level. There was a case in 2009 when a higher percentage of patients (70%) received thrombolytic therapy, which led to a marked decrease in the percentage of patients treated by conventional methods.
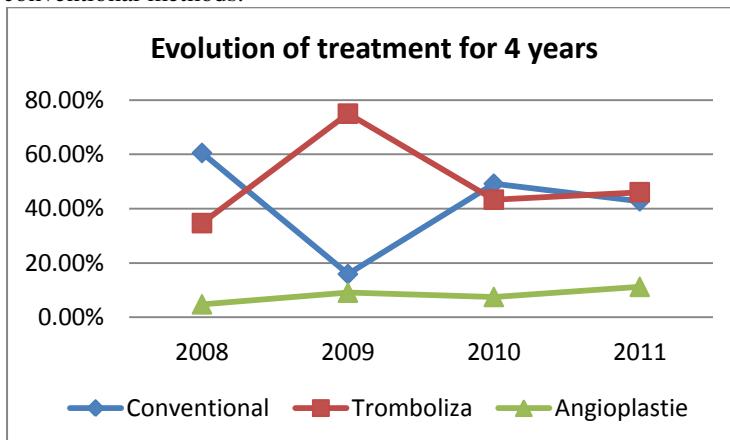
Figure VII.44 Evolution of treatment for 4 years

Conclusions

1. Age

The average age of occurrence of MI in men of Turkish-Tatar ethnicity is significantly lower than that of men in the general population.

In female patients are not observed statistically significant differences in terms of age distribution between the two groups.

2. Annual distribution of patients

The biggest difference between the two groups is found in September, when the Turko-Tatars percentage of patients is significantly higher than the percentage of the general population.

3. Circadian distribution of onset of pain

According to the results obtained there can not be said that there is a statistically significant difference in the circadian distribution onset of pain among the general population and the population of Turkish-Tatar origin.

4. Circadian distribution of admissions

There is no statistically significant association between patient ethnicity and hospitalization time.

5. Distribution of the interval from the onset of chest pain until admission

It was noted that there is a statistically significant association between ethnicity and the interval between onset of pain and delay in admission.

5.1 Distribution of the interval from the onset of chest pain until admission by gender

It was confirmed that there is a statistically significant association between sex of patients and range from pain onset to admission.

5.2 Distribution of the interval from the onset of chest pain to admission and gender - compared between the two groups

A statistically significant difference only appears if the interval from 144 to 168 hours, with significantly more cases where Turkish-Tatar population, however, the percentage does not exceed 5% of cases.

5.3 Pain onset interval - admission by age

Regarding the patients in the general population by applying the chi-square test is observed a statistically significant difference in the elapsed time between pain onset to admission according to age group.

In the Turko-Tatar ethnic population there is no statistically significant association between age group and the interval between onset of pain and hospitalization.

6. Hypertension

So it can be said with a high degree of confidence that the Turkish-Tatar patients in this study, aged less than 60 years, the more likely to suffer from hypertension than those in the general population.

7.Smoking

There is no statistically significant association between patient ethnicity and smoking.

8. Dyslipidemia

Turko-Tatars have dyslipidemia in a significantly higher percentage than the general population.As they age, Turkish Tatars shows less chance of developing dyslipidemia.The probability that a patient of Turkish Tatar ethnic who suffered a ST elevation MI to submit dyslipidemia is 1.4 times higher than for a person in the general population.

9. Diabetes

It can be stated with a high degree of confidence that the chances of a person of Tatar Turkish ethnicity suffering acute myocardial infarction with ST-segment elevation of suffering from diabetes are approximately 1.5 times higher than those of the general population.

10. Obesity

There is no statistically significant association between ethnicity and the presence of obesity in patients in this study.

11. Old myocardial infarction

There is a link in the history of IM and ethnic group originating patients.

12. Infarcted area

Tatar Turkish patients suffering from high tensile IM with a rate significantly higher than patients in the general population.

13. Killip class

It is noted that the percentage of patients with AMI Killip class III and IV is approximately equal for the two groups

studied. Observed distribution is homogeneous, so thereare no statistically significant differences between the two groups.

14. Treatment

From the analysis it can be concluded that streptokinase was prescribed to older patients and fibrin specific fibrinolytic to younger patients.

Streptokinase treatment regimen most commonly used is 1.5 SK MU/60 min

System used is sk least 0.75 in 10 min, the only mode specified in the ESC guidelines for the treatment of AMI.

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