ROMANIAN SOCIETY OF CARDIOLOGY
ACUTE CARDIAC CARE WORKING GROUP



RO-STEMI

THE FIRST ROMANIAN REGISTRY FOR ST-ELEVATION MYOCARDIAL INFARCTION (1997-2009)

FINAL REPORT

AMALTEA MEDICAL PUBLISHING HOUSE
www.amaltea.ro

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This report was published with the financial support of the MEDOCHEMIE Company and of the Romanian Society of Cardiology.

The MEDOCHEMIE Company had not any contribution and did not influence the content and the form of presentation of this document.

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ISBN 978-973-162-068-8

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A present without a past is bereft of a future
Nicolae Iorga

We are harboring the hope that the
data reviewed in this Report,
and which especially cover the first decade
of the 2000s, will be a good comparison base
for the efforts of future generations

We wish you success!

In memoriam: Dr. Dan Burghina

Foreword

The present report summarizes the data obtained in the interval 1 January 1997 – 31 December 2009 in 19510 patients with myocardial infarction, included in the first romanian registry for ST-elevation myocardial infarction (*Romanian Registry for ST-elevation Myocardial Infarction,* **RO-STEMI**).

A first attempt at a national registry on this subject was made in 1995. The starting point was the data base created in 1991 in the Coronary Care Unit of the Emergency Clinical Hospital "Floreasca", Bucharest. In 1995, the data accumulated to date were transferred onto an electronic support by a team including Cristina Teodorescu, MD, Aurelia Bumbu MD, Valentin Chioncel, MD, Stelian Cornaciu, MD, Alexandrina Fluerasu, MD, and Luminita Serban, MD, all, at the time, resident physicians. This group, later joined by Nicu Gainoiu, MD, Alexandra Diaconeasa, MD, Diana Zamfir, MD, Raluca Jumatate, MD, Ioana Bejan, MD, and Silvia Stavarache, MD, has also decisively contributed to the centralizing of data accumulation along the years. The database thus obtained has served as a model for an ampler database, created and distributed to the main Cardiology Departments in Romania with the support of the Merck, Sharp & Dohme Pharmaceutical Company, through the intermediary of Dr. Radu Vasilescu. However, this initiative has failed to capture the expected interest at that time.

RO-STEMI appeared in 1997 through the conjunction of efforts in three centers (Emergency Clinical Hospital "Floreasca", Bucharest, Municipal Hospital, Roman and County Emergency Hospital, Braila). Dr. Victor Firastrau had started as early as 1995 the centralization in a separate database of the data obtained in STEMI patients admitted to the Cardiology Department in the Roman Municipal Hospital. All these patients (as well as the subsequent ones) were progressively introduced into the "Floreasca" Hospital database. In turn, the colleagues from the Braila Emergency Hospital (at the time, the "Sfantul Spiridon" Hospital), led by Dr. Bogdan Minescu, have adopted the same database, provided to them by Dr. Luminita Serban, who had joined their team at that time.

At the beginning of RO-STEMI, including all infarction patients, regardless of type and chosen therapy, was a difficult proposition. For that reason, in 1997 and 1998, the registry was strictly restricted to thrombolysed patients, and followed two aims: 1 – a comparison of the effects and

prognosis of the different thrombolytical regimens, especially with two accelerated Streptokinase regimens; 2 – assessment of efficacy and tolerability of Enoxaparin (as compared to UFH) in thrombolysed STEMI patients.

In 1999, the registry was joined by the colleagues from the Constanta County Hospital (Prof. Dr. Elvira Craiu) and the Timisoara Municipal Hospital (Dr. Daniel Burghina, and subsequently, Prof. Dr. Mirela Tomescu). Doctor Burghina, reaped from us in an untimely manner, was one of the most active participants in the registry, and his efforts led to a high number of enrollees. This report is dedicated to his memory. All five above-mentioned centers had a constant contribution, which was essential for the formation and completion of the registry. 1999 also saw the adhesion to RO-STEMI of the Sfantul Pantelimon Emergency Hospital, Bucharest (Prof. Dr. Marius Vintila, Dr. Adrian Nechita, Dr. Tudor Protopopescu), with an important contribution up to 2007.

Starting in 2000, the number of the centers has progressively increased. Simultaneously, the investigators have started, out of their own initiative, to enter into the common database both thrombolysed and conventionally treated patients. The increase in the patient number was made possible, on one hand, by the fact that we have taken over the central database – "Bagdasar-Arseni" Emergency Hospital, Bucharest (Prof. Dr. Crina Sinescu, Dr. Eduard Ovricenco), Bucharest Municipal Emergency Clinical Hospital (Prof. Dr. Dragos Vinereanu, Prof. Dr. Mircea Cinteza), Cardiovascular Emergency Institute "C.C.Iliescu" Bucharest (Prof. Dr. Carmen Ginghina, Prof. Dr. Cezar Macarie), Brasov County Hospital (Prof. Dr. Mariana Radoi, Dr. Diana Tint); on the other hand, a significant amount of data was obtained by the transfer of locally processed data, as for instance in the Sibiu County Hospital (Prof. Dr. Ioan Manitiu); The County Hospital, Targu Mures (Prof. Dr. Imre Benedek) coordinators of their own national database; The "Nicolae Stancioiu" Cardiovascular Disease Institute in Cluj-Napoca (Prof. Dr. Radu Capalneanu, Dr. Stefan Mot); and of the 469 patients enrolled in 2007-2008 in the IMA-RO registry (Prof. Dr. Maria Dorobantu, Dr. Lucian Calmac).

2001 has marked the inclusion of the first RO-STEMI patient treated with primary angioplasty. The percentage of such patients has increased starting in 2004, thanks to the collaboration of the "Nicolae Stancioiu" Cardiology Institute in Cluj-Napoca; of the Targu Mures County Hospital; of the "Floreasca" Emergency Hospital, Bucharest; of the Cardiovascular Emergency Institute "C.C.Iliescu" Bucharest; of the "Prof. Dr. George Georgescu" Cardiology Institute Iasi (Prof. Dr. Catalina Arsenescu-Georgescu); of the Cardiovascular Disease Institute Timisoara (Prof. Dr. Stefan I. Dragulescu, Prof. Dr. Lucian Petrescu, Dr. Constantin Luca); of the University Municipal Emergency Hospital Bucharest; of the Cluj-Napoca County Hospital (Prof. Dr. Luminita Vidi-Simiti, Conf. Dr. Dan Olinic), and, starting in 2009, of the Private ICCO Clinical Centre, Brasov (Dr. Florin Ortan).

In 2003, the Registry was formally adopted, under its current name, by the Acute Cardiac Care Working Group of the Romanian Society of Cardiology. As a result of the effort of this Task Force, RO-STEMI has marked, since 2004, an even more rapid increase in enrollment, both as a result of

the input of centers with a medium or high volume of cases, (over 100 enrolled patients): The Oradea County Hospital (Senior Lecturer Dr. Katalin Babes), the Cardiology Centre, Craiova (Prof. Dr. Dan Dominic Ionescu, Dr. Constantin Militaru), The Arad County Hospital (Dr. Codin T. Olariu, Dr. Ileana Olariu), The "Sfantul Spiridon" Hospital, 1st Medical Cardiology Clinic, Iasi (Prof. Dr. Dan Mihai Datcu, Dr. Antoniu Petris), The Targoviste County Hospital (Dr. Mircea Vladoianu), the Baia Mare County Hospital (Senior Lecturer Dr. Calin Pop), The Targu Mures Centre for Cardiology and Transplant (Prof. Dr. Dan Dobreanu), The Hospital "Sfintii Doctori Fara de Arginti Cosma and Damian" Radauti (Dr. Paul Stancilescu, Dr. Doru Iliescu), The County Hospital Ramnicu Valcea (Dr. Ilie Petrescu), The Clinical Emergency Hospital "Sf. Apostol Andrei" Galati (Dr. Eugenia Nechita), The Pitesti County Hospital (Conf. Dr. Adrian Tase, Dr. Daniel Blejan) – and as a result of the input of centers with a lower volume: The "Dr. Fogolyan Kristof" County Emergency Hospital Sfantu Gheorghe (Dr. Lacramioara Topolnitchi), The "Acad. Prof. Dr. N. Cajal" Caritas Clinical Hospital Bucharest (Prof. Dr. Tiberiu Nanea), The Army Clinical Centre for Emergencies and Cardiovascular Disease, Bucharest (Dr. Liviu Chiriac, Dr. Vasile Greere), the Targu Neamt Municipal Hospital (Dr. Smaranda Garbea), The Colentina University Clinical Hospital, Bucharest (Prof. Dr. Dan Andrei Dan), The Targu Jiu County Emergency Hospital (Dr. Ion Malaescu), The Ilfov Clinical County Emergency Hospital Spitalul (Conf. Dr. Horia Balan, Dr. Alice Balaceanu), the Slatina County Hospital (Dr. Mircea Andritoiu), The Sighetul Marmatiei Municipal Hospital (Dr. Ioan Balea), The Fagaras Municipal Hospital (Dr. Bogdan Ghencea), The Campia Turzii City Hospital (Dr. Gavril Ludusan), The Elias University Hospital (Prof. Dr. Doina Dimulescu), The Satu Mare County Hospital (Dr. Ladislau Kiss) and the "Ion Jianu" Military Hospital, Pitesti (Dr. Viorel Stanciu).

The RO-STEMI data were progressively accumulated and reviewed in scientifical papers presented both at the Meetings of the Romanian Society of Cardiology, and at international meetings, or published in peer-reviewed journals both in Romania and abroad, under different acronyms (RO-MAS, CLEXAS, ASENOX, ASK-ROMANIA). Some of the results were statistically processed and published in collaboration with colleagues from the Bologna, Italy University (Prof. Dr. Raffaele Bugiardini). Following the proposal of Prof. Dr. Dragos Vinereanu, in 2007, a RO-STEMI board was created, to cope with the increase both in the volume of accumulated information and in the number of investigators. This board includes representatives of the centers with more than 100 enrollees. The role of the board has been that of evaluation and approval for publication of proposals for scientifical papers based on the RO-STEMI database.

By the large volume of information, originating from centers spread across our national territory, the registry has progressively become a reflection of the demographic, therapeutic, and prognostic particularities of STEMI patients admitted over the past decade in Romanian hospitals. On this basis, in 2009, the Romanian Society of Cardiology has had the possibility to become involved, alongside the Cardiology Committee of the Health Ministry, in the elaboration of the National Programme for Primary Angioplasty in STEMI, implemented since August 2, 2010.

RO-STEMI could not have been finalized without the loyal, professional and moral support of several colleagues who were constantly close to the spirit of the Registry, ever since its beginnings. The names of these colleagues were mentioned in the first paragraphs of this Foreword. Similarly, RO-STEMI could have not existed without the smaller or greater effort of the 43 participating centers, which resulted in the enrollment of a number of patients higher than that of most national or international registries on this subject, across Europe. All the over 150 investigators (mentioned in a separate Appendix) are praiseworthy for their input during the 13 years of existence of this first RO-STEMI Registry.

Worthy of special mention are Dr. Alexandra Diaconeasa (Bucharest), for the tenacity with which she has ensured the maintenance of the database in the interval 2000 – 2008, and Dr. Antoniu Petris (Iasi), for the statistical processing of the large volume of data.

A special token of gratitude goes to those whose exquisite modesty has led them to refuse the mention of their names, despite their substantial input in data gathering and processing. The talent and patience of Dr. Raymond Ținț (Brasov), materialized in the creation of the RO-STEMI logo also require special mention.

Gabriel Tatu-Chitoiu, MD
RO-STEMI Coordinator

I. Introduction

Registries provide data from a large number of patients, regarding morbidity, demographic and clinical particularities, mortality, the degree of adherence of practicing physicians to the diagnostic and treatment guidelines generated by clinical trials, as well as regarding the manner in which existing resources are put to use. Registries can demonstrate differences in clinical practice between different geographical regions or even within the same geographical region and, if carried out over the long term, they can demonstrate trends of change for the different parameters to hand, such as risk factor dynamics, or changes in the therapeutic attitude. Thus, registries can have an important contribution in changing strategies of general or specific Health Care policies regarding a specific disease (1).

Registries can be considered as the link between randomized clinical trials and everyday practice (1), and this is well illustrated by data gathered along the years regarding acute STEMI. The results of randomized trials dealing with STEMI during the past two decades have suggested that the new therapeutic approaches can reduce short-term mortality mortality down to remarkably low levels (around 6-7 percent). For instance, 30-day mortality, as reported in the GUSTO-I trial, was of 6.9%. However, in patients not considered eligible for this trial, mortality was 16.8%, i.e., larger than double that in randomized patients. Moreover, the mortality shown by STEMI registries varies between 15 and 20% (4). Patients enrolled in randomized trials were younger, included relatively lower numbers of females, and had lower co-morbidities (3). These particularities go a far way in explaining the discrepancy between the optimistic trial data and the data recorded in the registries. As a result, according to some, the results of randomized trials cannot be used in clinical practice in up to 50% of patients (1). Clinical registries can fill in the gap between the ideal results of randomized trials and everyday reality.

While, over the past two decades, cardiovascular mortality has shown a trend toward decrease in Western and Central Europe, reaching values as low as 3-5 fatalities per 1000 inhabitants in 2003, in Romania the tendency was completely opposed, reaching up to 8 fatalities per 1000 inhabitants in the same year. This tendency was only second to that seen in Bulgaria, the Ukraine, and, especially, in countries belonging to the ex-Soviet Union (5). Data from 2008 point out to Romania as belonging to the group of countries with the highest mortality caused by ischemic heart disease or cerebrovascular disease (Figure 1). For the interval 2000-2008, the present registry

has noted a global in-hospital mortality of 13,5%, a value placing Romania on the last place but one in Europe, as shown in a multinational analysis published in 2010 (7) (Figure 2).

The analysis of this phenomenon regarding Romania has been very difficult, due to a virtual lack of information. For instance, the MONICA project of the World Health Organization, dedicated to the monitoring of cardiovascular risk factors and mortality has included only a few East-European countries: Russia, ex-Yugoslavia, Poland, ex-Czechoslovakia, Hungary and the ex-German Democratic Republic (8). At that time, there existed a MONICA centre in Romania (centre 53, coordinated by Prof. Dr. Carmen Ginghina, and following up patients from Bucharest's Sector II)(9). Geographically, Romania is the largest country in southeastern Europe, has a relatively large population, and important natural resources (10). Nevertheless, from certain points of view, Romania was and still is a "forgotten country". Only few studies evaluating cardiovascular risk factors included Romania. Thus, only four trials referring to STEMI included patients from Romania (11-13), and the number of these patients was too low to allow subgroup analysis.

In this context, the Romanian registry for the ST-elevation myocardial infarction tries to outline an image of the reality faced by our country in the interval 1997 – 2008, relating to this condition. We hope that the publication of the registry, a result of the coordinated efforts of over 150 investigators, will bring a substantial contribution to canceling the status of a "forgotten country" for Romania.

As compared to the preliminary data published in 2009 in the Romanian Journal of Cardiology (14), the current report includes data for 2009, additional data for 2004-2009 for interventionally-treated patients from the "Niculae Stancioiu" Heart Institute, Cluj-Napoca, and data for 2004-2009 from the Regional Infarction Registry coordinated by the Targu Mures County Hospital. The report also includes three additional analyses (comparative data between economical regions; between thrombolytic regimens; and between patients treated conservatively, interventionally, or by thrombolysis).

II. Methods

II.1. Patients eligible for RO-STEMI

RO-STEMI has included patients with classical diagnostic criteria:

- Clinical criteria: Severe, prolonged pain, over than 15-20 minutes, localized retrosternally or in the epigastrium, with or without radiation to the left shoulder and/or left upper limb and/or neck and/or left interscapulovertebral space, not responding to nitroglycerin.
- ECG criteria: ST elevation ≥ 0.2 mm in V2-V3, and/or ≥ 0.1 mm in other leads, or new-onset LBBB.
- Laboratory criteria: pathological increases in the CK/CK-MB levels; in later years, fields for troponin levels were added to the database.

II.2. Data acquisition

Data acquisition from RO-STEMI patients was carried out in two manners:

1. Inclusion in the common database

The structure of the common database has suffered several changes, prior to reaching its final form, which was conceived in Microsoft Office Access 2003 (1985-2003 Microsoft Corporation). For easier data acquisition, the information was encoded whenever possible; encoding or decoding of a specific field is directly visualized on the computer screen. For users unfamiliar with Microsoft® Office Access, a version was created in Microsoft® Office Excel 2003 (1985-2003 Microsoft Corporation).

Patient inclusion in the database was performed either directly, by the investigators, or indirectly, by the registry coordinator, by inclusion of data originating from other databases. Such was the case of the 469 patients enrolled between the years 2007-2008 in the IMA-RO myocardial infarction database (coordinators, Prof. Dr. Maria Dorobantu and Dr. Lucian Calmac), and of the 231 patients from 1997-2009, originating from the Roman County Hospital (Dr. Victor Firastrau).

The data included in the registry refer to: ID, demographics, coronary risk factors, infarction location, Killip class on admission, time to admission and to treatment initiation, in-hospital therapy (conservative or interventional), STEMI complications, complications of treatment, and mortality. All these data were accessible to all the centers and were considered mandatory. Given the

limited access of some centers to certain procedures, the database was elastic, allowing additional details to be acquired only by those centers capable of doing so. For instance, some centers have the possibility to graphically record the dynamics of the ST segment and of the T and Q waves, in patients treated with reperfusion therapy. In these centers, the protocol mandated recording ECG tracings at 15-minute intervals in the first 180 minutes of reperfusion therapy initiation. In these patients, remission of the thoracic pain within 180 minutes of thrombolysis initiation, associated to a greater than 50% reduction of the sum ST segment elevation within 180 minutes, with or without arrhythmia suggestive of reperfusion, were considered as ECG reperfusion criteria. The dynamics thus recorded were classified into three ECG types suggestive of reperfusuion, and mentioned in a special field, adopted by some of the centers.

Some of the centers have the possibility to follow up myocardial enzyme dynamics by serial measurements, carried out before and after the beginning of therapy, at 4,9, 12, 16, 20, 24, 48, 72, and 96 hours. The data thus obtained were introduced in a registry sub-folder. However, it is rapid increase of the CK/CK-MB, peaking in the first 12 hours from reperfusion initiation, that has served as the overall lab criterion for successful thrombolysis.

2. Processing of locally acquired data

Alongside directly included data, the current report also includes directly acquired data, either in STEMI tables provided some centers (County Hospital Targu Mures for the interval 2004 – 2009, and, for 2008, the County Hospitals in Oradea and Sibiu), or according to the clinic's own criteria and format, as in the "Prof. Dr. Niculae Stancioiu" Heart Institute in Cluj-Napoca. For logistical reasons, the follow-up period was limited to the hospitalization period.

II.3. Data centralizing

Information was sent periodically by the investigators to the RO-STEMI coordinator. Data were transmitted initially on electronic support, and subsequently, via Internet. Data quality was analyzed at reception. In the event of a major error or of unclear components, the file was returned to the investigators, together with the relevant remarks; data were accepted when properly presented and added to the central database. The final central database, obtained after the introduction of all the data obtained up until 31 December 2009, was subsequently meticulously checked, by two separate investigators, to eliminate potential incompatibilities between the different fields. Similarly, the central database was, in its entirety, checked and corrected in respect of data quality.

For faster data centralization, the final central database was separated for each of the years of the RO-STEMI follow-up. The 13 annual sub-folders were distributed each to a RO-STEMI investigator who had actively participated in data introduction at least over the corresponding year, and was familiar with the database structure. The investigator centralized the annual data in single,

prespecified tables. The annual data thus obtained, sent to the RO-STEMI coordinator, were used for establishing the dynamics of the different RO-STEMI parameters, over the 13 years of follow-up. The global RO-STEMI data were directly accessed from the central database.

II.4. Statistical analysis

The data were analyzed using the SPSS 15.0 for Windows program (LEAD technologies, Inc.). The analysis and interpretation of the annually centralized data and of the global data, as well as the statistical analysis of the data was carried out, independently and comparatively, by two investigators. The frequency of a given RO-STEMI variable was evaluated strictly in the patients in whom the existent data were validated, using the formula X = n / (total patient number– patients ND), where X signifies frequency, n= the number of patients fulfilling the criterion, and ND, "no data"; the latter applied to patients where it was not known whether the criterion was fulfilled or not. For instance, the dynamics of STEMI occurrence over the 24 hour span was reported strictly for the patients with a clearly reported onset time, which was not the case for all patients. Similarly, the degree of utilization of anticoagulation, antiplatelet, statin, beta blockers, and ACE-inhibitor therapy was carried out excluding "ND" patients.

The results are presented as proportions, mean +/- SD, and median. For the comparison of mean values, we used the *t*-test, and for comparison of the proportions, we used the chi square test. Statistical significance was considered to be present with $p< 0.05$.

II.5. Data presentation

The graphic presentation of the data and the writing of this text were performed by the investigators who also carried out the statistical analysis. The material thus obtained was sent to and approved by the members of the RO-STEMI Board, which includes representatives of the centers who enrolled a minimum of 100 patients into the database.
The current report focuses on analysis of both general and comparative data (economic regions, thrombolytic regimens, conservative vs. thrombolytic vs. interventional therapy). Additional analyses, specific to certain patient subgroups, are currently being prepared by several investigator teams, and will be published as separate papers.

III. Results

III.1. Participating centers

The data analyzed in the current report originate from 43 centers, with a territorial distribution as presented in Figure 3. The number of centers active for each year in the interval 1997-2009 is shown in Figure 4. The complete list of the participating centers, in the chronological order of their adherence to the registry, as well as the annual contribution of each centre is presented in Table 1.

Centers included 18 traditional university hospitals (41.86%), 16 county hospitals, of which 5 became university hospitals over the past few years (37.20%), 6 municipal or city hospitals (13.95%), 2 military hospitals (4.65%), and 1 private hospital (1.32%) (Table 2 and Figure 5).

We considered it useful to present some of the RO-STEMI data comparatively, according to the 8 Development Regions of Romania. These are territorial and statistical units resulting from the free association of County Councils, and represent the centers for collection of specifical statistical data at the territorial level, as well as the framework for the elaboration, implementation, monitoring, and evaluation of the strategies for regional development and of the corresponding programmes for economic and social cohesion (15).

The 8 regions are at the base of the Regional Operational Programme 2007–2013 (POR), and were established by Law nr. 151/1998 for regional development, modified by Law nr. 315/2004, in accordance with the CE Rule Nr. 1059/2003, referring to the establishment of a common system for statistical classification of the territorial units.

These Development Regions (Figure 6):

- **Region 1: North-East (Moldavia)** includes 6 counties: Bacau, Botosani, Iasi, Neamt, Suceava and Vaslui.
- **Region 2: South-East (Lower Danube)** includes 6 counties: Braila, Buzau, Constanta, Galati, Tulcea and Vrancea.

- **Region 3: South (Muntenia)** includes 7 counties: Arges, Calarasi, Dambovţa, Giurgiu, Ialomita, Prahova and Teleorman.
- **Region 4: South-West (Oltenia)** includes 5 counties: Dolj, Gorj, Mehedinţi, Olt and Valcea.
- **Region 5: West (Apuseana)** includes 6 counties: Arad, Caras Severin, Hunedoara and Timis.
- **Region 6: North-West (Someseana)** includes 6 counties: Bihor, Bistriţa-Nasaud, Cluj, Maramures, Satu Mare and Salaj.
- **Region 7: Centre (Mureseana)** includes 6 counties: Alba, Brasov, Covasna, Harghita, Mures and Sibiu.
- **Region 8: Bucharest–Ilfov** includes Bucharest and the Ilfov county.

Table 3 shows some of the indicators for regional development in Romania, according to official data from 2005-2006. Discrepancies between the GNP in the Development Regions can be observed, as well as differences in the number of ambulances and of angiographic procedures (these indicators are the best represented in regions 5,6,7 and 8).

Figure 7 illustrates the territorial distribution of RO-STEMI centers according to the Development Regions, and Figure 8 indicates the percent participation of each region in the RO-STEMI registry.

The ten Bucharest centers represent 23.5% of the total 43 participating centers, and cover a population of 4,000.000 (i.e., the population of Bucharest and of the adjacent counties), or approximately 25% of Romania's population. The RO-STEMI centers from Regions 6 and 7 each represent 16.26% of the total; Region 1 centers represent almost 12%, Regions 3 and 4 represent 9.30 each, and Regions 2 and 5 represent 6.97% each (Figure 8).

III.2. RO-STEMI patients

A total number of 19,510 patients were included in this report, as follows:

1. a group of 15,483 patients (79.35%), whose data were prospectively entered into the registry by the investigators, in the interval January 1, 1997 – December 31, 2009; this group included 469 patients (3.03%) with RO-STEMI-compatible data from the IMA-RO registry;
2. a group of 1939 patients (9.93%), entered in the interval 2004-2009 in the Regional Infarction Registry coordinated by the Targu Mures County Hospital, using RO-STEMI prespecified tables;
3. a group of 586 patients (4.00%) admitted to the County Hospitals Oradea (315 patients) and Sibiu (271 patients), for whom these two centers organized the local statistical data in prespecified RO-STEMI tables;

4. a group of 1502 de patients (7.69%) treated interventionally at the "Niculae Stancioiu" Cluj-Napoca Heart Institute, and processed according to the Institute's own criteria and format (Table 4).

The annual enrollment of patients in the registry was higher after the year 2000, and especially after the year 2004, with a peak in the year 2006 (Table 1 and Figure 9). Figure 10 presents the evolution of the cumulative enrollment rate. Of note, in 1997 and 1998, only thrombolysed patients were enrolled, from three centers only.

Of a total of 19,510 RO-STEMI patients, 13193 were admitted in traditional university hospitals (67.61%), 5578 in county hospitals, (28.59%) 466 (2.39%) in municipal or city hospitals, 70 (0.35%) in the two military hospitals, and 201 (1.03%) in one private hospital (Table 5 and Figure 11).

The degree of representation of the different Development Regions was the following: region 1: 1149 (5.88%); region 2: 1656 (8.48%); region 3: 452 (2.31%) (many of these treated in Bucharest hospitals); region 4: 747 (3.82%); region 5: 1703 (8.72%); region 6: 2701 (13.84%); region 7: 4157 (21.30%); region 8 6945 (35.59%) – Table 6 and Figure 12. Table 7 shows the annual enrollment rate for each region.

III.3. Monthly and daily RO-STEMI patient distribution

The percent monthly distribution of STEMI patients could be identified in 14145 (72.50%) cases. In these patients, was most frequent in March, April, and May (for a total of 3973 patients, 28.08%), the least admissions were seen in July, August, and September (3027 patients, 21.49%).

The difference between the number of hospitalizations for infarction was, for the two intervals, strongly significant statistically ($p< 0.0001$). The distribution of hospital admissions in other months of the year was relatively constant, between the two above-mentioned extremes (Table 8, Figure 13).

The daily distribution of STEMI patients was analyzed from two standpoints: 1 – the time of symptom (chest pain) onset; 2- the time of hospital admission. The time of STEMI onset was recorded in 11743 patients (60.18%). The highest frequency (23.73%) was recorded between 8:00 AM and 11:59 PM ($p< 0.0001$ for the comparison to any of the other five time intervals).

The lowest STEMI onset frequency was noted at 20:00-23:59 and 0:00-3:59, the noted values (15.39% and, respectively, 15.83%) being significantly lower than any other daily time interval ($p< 0.0001$). (Table 9 and Figure 14).

The time of admission was correctly entered in 11408 (58.47%). The frequency of hospital admissions was highest between 08:00–15:59, significantly higher than any other interval. The lowest frequency of hospital admission for STEMI was noted at 0:00-7:59, with values significantly lower as compared the afternoon and evening hours ($p< 0.001$) (Table 10 and Figure 15).

III.4. Patient transport to the hospital

The modality of transportation to the hospital was recorded in 10919 patients. Approximately 84% of these were taken to the hospital by ambulance. Conversely, more than 15% (practically one patient out of six) reached the hospital by private transportation. 14 patients used public transportation (0.10%), 6 (0.05%) walked to the hospital, and 2 (0.02%) were brought in by mobile police squads. In 106 patients (0.97%), STEMI onset occurred during another hospitalization (Table 11 and Figure 16).

III.5. The onset-to-admission time

The time of infarction onset was determined based on the patient's and/or their companion's account. The time lag between symptom onset and hospitalization could be determined in 12479 patients (63.96%), 8701 (69.72%) males and 3778 (30.28%) females. Globally, the time median for the pain onset/hospitalization gap was of 240 minutes. However, this should not be equivalent to the time lag between infarction onset and the presentation to the emergency room, which could not be identified but was, doubtless, considerably shorter. The pain-to-hospitalization time includes the pain-to-emergency department time plus the time spent in the emergency department, until the diagnosis is established and the decision for hospitalization is made.

A group of 4580 patients (36.69%) were admitted in the first 3 hours from onset, and 3385 (27.12%), were admitted at 3-6 hours. Thus, two-thirds of patients were admitted during the first 6 hours from infarction onset, i.e., during the optimal window of opportunity for the initiation of coronary reperfusion therapy. Another 1745 patients (13.98%) were admitted at 6 -12 hours, and 1115 (9.21%), at 12-24 hours from onset. Conversely, 1654 patients (13.25%) were admitted later than 24 hours, with 107 (0.80%) admitted later than seven days from onset (Table 12 Figure 17).

The median of the onset-to-admission time was clearly lower in men than in women (210 vs. 280 minutes). Nearly 40% of men were admitted within the first 3 hours of symptom onset, vs. 29% of women ($p < 0.0001$). After the first 3 hours, thus ratio reverted, in «favor» of women (Table 12 and Figure 18).

Elderly patients had an onset-to-admission time significantly longer than that of younger patients. Thus, 45% of patients under 45 de and 44% of 45-59-year old were admitted in the first 3

hours from onset, as compared to only 34% of 60-74-year olds, and 26% of over 75-year old ($p < 0.0001$ for the comparison between each of the first two, to each of the last two groups). Therefore, elderly patients became the main group admitted beyond 6 hours from onset (Table 13 and Figure 19).

III.6. The admission-to-treatment time

STEMI treatment was considered initiated when thrombolytic therapy was started or primary angioplasty was performed, or at the start of conservative (usually, anticoagulant) therapy. The time lag between the time of admission and initiation of treatment was recorded in 12,063 patients. Globally, the median admission treatment time was of 30 minutes. The treatment started during the first 30 minutes of admission in 5486 patients (45.47%), and in the second half hour from admission in 5198 patients (43.09%) (Table 14).

There were, however, differences between patient subgroups as regards treatment initiation. Thus, treatment was started in the first 30 minutes in only 42% of women, as compared to 47% of men ($p <0.0001$) (Table 14 and Figure 20). Furthermore, there was a "gradient" from younger to more elderly patients: thus, if 51% of patients under 45 were started on therapy within 30 minutes of admission, this was the case in only 47% of patients aged 45 – 59, 44% of those aged 60 – 74, and 43% of those over 75 (Table 15 and Figure 21). The differences between the admission-to-treatment times in patients treated conservatively, with thrombolytics, or by primary angioplasty are discussed below, under a separate heading.

III.7. Patient age and gender

Mean age was calculated based on 17422 patients. For patients from the Targu Mures County Hospital and the Cluj Napoca Heart Institute, the average age was calculated separately, and was correlated with the data from the main database.

The mean age of RO-STEMI patients was 63,39 +/- 12 (median, 63) years; 13376 were males (68.56%) and 6134 were females (31.44%) (Table 16 and Figure 22). The mean age for females was 6 years higher than that of males (67.43 +/- 12 and 60,92 +/-12 years, respectively, $p < 0.0001$).

The age-distribution pyramid (Figure 23) shows a male preponderance for all age groups below 75, the male/female ratio being markedly higher under 65 years.

For the entire follow-up period (1997 – 2009), the mean age for females was around 68, and that of men, around 60. For the first 2 years of observation, the mean age appeared to be lower, due to inclusion, in those years, of thrombolysed patients only. At that time, there was some hesitation

in treating thrombolytically patients over 75. The overall mean age over the entire period of observation was 62 years (Table 18 and Figure 24).

The mean ages by Development Regions are shown in Table 19 and in Figures 25, 26 and 27. We have analyzed the 8 Regions by grouping them according to the per capita GNP, as follows: Regions 1, 2, 3 and 4 (GNP per capita less than 2800 Euro); Regions 5, 6 and 7 (2800-5600 Euro); and Region 8 (over 5600 Euro) (Table 19).

This brought to the fore a significantly higher percentage of female patients in Regions 5, 6 and 7 (33.65%), as compared to Region 8 (30.56%, $p < 0.0001$) and to Regions 1, 2, 3 and 4 (28.53%, $p < 0.0001$). The difference between Region 8 and Regions 1,2,3 and 4 was also significant ($p < 0.0001$). The mean age was also significantly higher in Regions 5, 6 and 7 (63.71+/-11.19 years) than in Region 8 (62.0+/-13 years) and in Regions 1,2,3 and 4 (21.0+/-13) ($p < 0.001$ for all comparisons between the three groups).

These differences were noted in males (61.34+/-11.5, 60.0+/-13 and, respectively, 59.0+/- 12 years, $p < 0.0001$ for all comparisons between groups). However, the highest mean age for females was noted in Region 8 (69.0+/-12 years), significantly higher than the mean age in Regions 5, 6 and 7 (67.6+/-10.19) and that the mean of 67.0+/- 11 noted in Regions 1,2,3 and 4 ($p < 0.0001$ for both comparisons). The age difference was not found significant for the comparison between females from Regions 1,2,3 and 4 to those from Regions 5, 6 and 7 ($p = 0.105$) (Table 20 and Figures 28, 29 and 30).

These data allow to conclude that the mean ages in RO-STEMI patients (especially in males) were lower in regions with a per capita GNP lower, as compared to higher, than 2800 Euro. From another perspective, the mean ages were significantly higher in Northern than in Southern Romania.

III.8. Coronary risk factors

Hypertension was the most frequent coronary risk factor (52.36%). The incidence of hypertension was significantly higher than that of smoking (47.29%, $p< 0.0001$). The other risk factors were significantly less prevalent: dyslipidemia (39.44%), obesity (22.04%), diabetes (21.92%), and previous myocardial infarction (7.78%) (Table 21 and Figure 31). Table 22 shows the yearly incidence of the main coronary risk factors between 1997 – 2009, and Figure 32 displays the same data for the last decade.

A note should be made of the relatively constant incidence of hypertension (between 50-53%), of diabetes and obesity, around 20% (with co-variation of these two conditions), and of dyslipidemia (around 40%).

The incidence of smoking has decreased in 2004-2009, after having been relatively constant around 50% in the other years. However, the incidence of risk factors differed in by age group. Thus, smoking was by far the most frequent risk factor in patients younger than 60. After this age, the number of smokers decreased rapidly, and hypertension became the main risk factor.

Dyslipidemia was the second most frequent risk factor until the age of 50, and has decreased thereafter. The incidence of diabetes doubled between the ages of 40 and 55. Between the ages of 55 and 75, approximately one-quarter of RO-STEMI patients had diabetes (Table 23 and Figure 33).

III.9. Localization of myocardial infarction

Localization of myocardial infarction was anterior (large anterior, anterior, anteroseptal, or high lateral) in 51.63% of patients, and nonanterior (posteroinferior, inferior, true posterior or posterolateral) in 48.39%. (Figure 34).

III.10. Killip class on admission

This was mentioned in 16693 patients (85.56%), and the exact class was known in 15191 patients. From them, 10382 patients were in Killip class I (68.34%), 3682 in Killip class II (17.65%), 1205 in Killip class III (7.93%) and 922 in Killip Class IV (6.06%) (Table 24, Figure 35).

Table 25a shows the distribution of these patients in the 8 Development Regions. There is a variable distribution of Killip class IV patients, from 1.54% for region 3, up to 11.74% for region 6. However, it must be kept in mind that many of these latter patients are transported to Bucharest (region 8).

For the 1502 de patients interventionally treated at the Cluj-Napoca Heart Institute, reporting of classes III and IV was pooled. Thus, 14311 out of 16693 were reported to be in classes I and II (85.54%) and 2427 (14.46%), in classes III and IV. This mandated a separate analysis by pooling the Killip classes of the two groups, which allowed incoroporating the data (Table 25b and Figure 36). The same variability can be observed for patients in Killip classes III and IV, from 6.19% (region 3) to 20.86% (region 6) and 24.25% (region 5). This analysis is helpful for the comparison of global mortality in the 8 regions.

III.11. Treatment

III.11.1. Conservative therapy/Thrombolysis/Primary Angioplasty

The use of the different treatment modalities (thrombolysis, primary angioplasty, or conservative therapy) is shown in Table 26 and in Figure 37. Nearly half of the 19510 patients (9692) were

treated conservatively, 7234 (37.07%) received thrombolytics, and 2525 (12.93%) were treated by primary angioplasty. The type of treatment could not be identified in 59 patients (0.32%).

Table 27 and Figure 38 illustrate the ratio between the three treatment modalities in the 13 years of follow-up. For 1997 and 1998, RO-STEMI was strictly a registry of thrombolysed patients. Primary angioplasty as a therapeutic procedure first made its way into the registry in 2002.

Infrequent until 2007, the use of primary angioplasty has substantially increased over the last two years of the registry (from 14% to 30%).

Table 28 and Figure 39 show the therapeutic procedures used, by Development Region. Patients treated by angioplasty originated especially in region 6; in regions 1, 7 and 8; and (to a lesser extent) in region 5. Regions 2, 3 and 4 did not include interventionally treated patients.

Table 29 presents comparatively the main demographic characteristics of the patients treated conservatively, with thrombolytics, or by primary angioplasty. Conservatively treated patients had a higher mean age, included more females and Killip class III and IV patients, and had a significantly longer onset-to-admission time as compared to those treated with thrombolytics or by primary angioplasty ($p<0.0001$ for all comparisons). Thus, older age, higher Killip class, longer onset-to-hospitalization time and female gender were factors reducing the chance of a reperfusion treatment.

While the incidence of hypertension was similar in all three groups of patients, the number of smokers and of dyslipidaemic patients was lower among conservatively treated patients ($p<0.0001$). Of note, the percentage of smokers of dyslipidaemic patients was significantly higher in the group treated with primary angioplasty as compared to that treated with thrombolytics (table 29).

Out of 7234 patients treated with thrombolytics, 4510 received streptokinase, 961 alteplase (tPA), 1119 reteplase (rPA) and 400 tenecteplase (TNK). In 244 patients, the thrombolytic agent could not be identified (as a general rule, due to participation in a double-blind study).

In the patients treated with thrombolysis, a progressive shifting from streptokinase to fibrin-specific thrombolytics was noted over the 13 years of the registry. Thus, if in the first two years, streptokinase was the only thrombolytic agent used, the number of patients thus treated gradually decreased, so that in 2008, the ratio was reverted, in favor of fibrin-specific agents (Table 30, Figure 40). The first patients treated with alteplase were seen in RO-STEMI in 1999, reteplase was first noted in 2000, and tenecteplase, in 2004.

The main characteristics of patients treated with thrombolytics are shown in table 31. The mean age of patients treated with streptokinase was by three years higher than that of patients treated with alteplase or reteplase and by one and a half years higher than that of patients treated with tenecteplase, (significant differences, $p < 0.0001$). In this manner, the percentage of patients with ages equal to or higher than 75 was significantly higher in the group treated with streptokinase (12.26%) as compared to that treated with alteplase (6.87%), reteplase (6.87%) or tenecteplase (8.50%).

The incidence of hypertension, smoking, and dyslipidaemia was significantly lower in patients treated with streptokinase as compared to patients treated with specific fibrinolytics. The incidence of diabetes was lower in patients treated with streptokinase (18.74%) or alteplase (17.17%) as compared to those treated with reteplase (20.20%) or tenecteplase (23.25%). Globally, there were no significant differences between the four groups as regards the incidence of Killip class III and IV.

Table 31 demonstrates that streptokinase was preferred in older patients, while fibrin-specific fibrinolytics were preferred in younger patients. In patients treated with streptokinase, different regimens were used. Thus, 1700 patients received streptokinase 1.5 Megaunits (M.U.) over 60 minutes, 793 patients 1.5 M.U. in 30 minutes, 828 patients 1.5 M.U. in 20 minutes, 818 patients 0.75 M.U. in 10 minutes (in 162, a second dose of 0.75 MU was given in 10 minutes if after 50 minutes there were no ECG signs of coronary reperfusion), 182 patients received streptokinase 0.75 M.U. in 15-20 minutes, 24 received 0.75 M.U. in 60 minutes, and in 9 patients streptokinase was combined with alteplase. In 156 patients the streptokinase regimen was not noted.

As mentioned, fibrin-specific fibrinolytics were introduced in clinical use later than streptokinase; therefore, we compared mean ages and incidence of Killip classes III and IV in patients treated with fibrinolytics in the last five years of follow-up (2005 – 2009), when all agents were frequently used in all groups of patients (Table 32). The highest mean age (62+/-13 years) was noted in patients treated with streptokinase 0.75 M.U. infused over 10-15 minutes. Excepting the comparison to the classical regimen of 1.5 M.U./60 minutes, this mean age was significantly higher than the mean ages noted in the other subgroups ($p=0.023$ for the comparison to streptokinase 1.5 M.U./30 minutes and $p < 0.0001$ for comparisons to streptokinase 1.5 M.U./20 minutes and, respectively, tPA, rPA and TNK). In turn, the mean age of patients treated with streptokinase 1.5 M.U./60 minutes was significantly higher than the mean ages of patients treated with streptokinase 1.5/20 min, rPA and tPA ($p < 0.0001$ for all comparisons) and as compared to TNK ($p=0.005$), but unsignificantly higher than the mean age of patients treated with streptokinase 1.5 M.U./30 minutes ($p=0.188$).

Finally, the age of patients treated with streptokinase 1.5 M.U./30 minutes was unsignificantly higher as compared to patients treated with TNK, but significantly higher as compared to patients treated with rPA, tPA ($p<0.0001$ for both comparisons) or treated with streptokinase 1.5M. U./20 minutes ($p=0.030$). Thus, for fear of haemorrhagic complications, cardiologists appear to have preferred, in older patients, either one-half of the streptokinase dose given more rapidly, or the classical, slower streptokinase regimen (1,5 MU/60 minutes), while in younger patients, fibrin-specific fibrinolytics or an accelerated regimen for the classic dose of streptokinase (1.5 M.U./20 minutes) were used.

Additionally, the streptokinase regimen of 0.75 M.U./10 minutes was used more frequently in patients in Killip class III or IV (12.39%). The difference was was significant for the comparison between this subgroup and patients treated with streptokinase 1.5 M.U./30 minutes ($p=0.027$) , and close to significance for comparisons to streptokinase 1.5M.U./20 minutes ($p=0.057$) and TNK ($p=0.067$)(table 32).

III.11.2. Anticoagulants, antiagreggants, beta-blockers, ACE-inhibitors, statins

The utilization rate of the main STEMI drug classes (anticoagulants, antiaplatelets, beta-blockers, ACE-inhibitors, statins) was recorded in more than 85% of patients (varying between 85% for statins, i.e., 16619 patients, and 90% for antiagreggants, i.e., 17584 patients) (Table 30, Figure 41).

Anticoagulants

Use of anticoagulation has been relatively constant over the 13 years of observation, at about 95% (Table 33, Figure 41). The global rate was 94.74% (Table 33 and Figure 42).

Over the last 10 years of the follow-up, a reversal was noted among the main components of the anticoagulant therapy. Table 34 and Figure 43 reveal that enoxaparin was only second to unfractionated heparin (UFH) in the frequence of use, and has gradually started replacing UFH after 2002.

Starting in 2006, a new tendency was noted: the utilization of a combination between UFH (during the Intensive Coronary Unit stay) and enoxaparin (after discharge from this Unit). Thus, after the year 2008, the number of patients treated with enoxaparin alone or associated with UFH has exceeded that of patients treated with UFH only. In 2009, 70% of patients were treated by one of these two methods of anticoagulation.

From 2006 onwards, other anticoagulants (especially Fondaparinux) started being used (Table 34 and Figure 43).

Antiplatelets

Antiplatelets the administration rate for antiplatelets has been constant, at around 90%, between 1997 and until 2006. Between 2007-2009, approximately 98% of patients received antiplatelets (Table 33, Figure 41). Aspirin was, practically, the only antiplatelet agent administered until 2002. Starting that year, the use of dual antiplatelet therapy (Aspirin and Clopidogrel) increased rapidly. Thus, in 2008, almost 80% of patients received this combination. GP IIbIIIa inhibitors use was low, even lower than that of primary angioplasty (Table 35, Figure 44).

Angiotensin Converting Enzyme Inhibitors (ACEIs), beta-blockers and statins

The global rate of use for these was of 72.14%, 71.14% and, 66.92%, respectively. For ACEIs and beta-blockers, a first increase was noted from 40% to 70% in the interval 1999-2001, and this value has remained relatively stable until 2005. The year 2006 has seen a new increase of the administration rate for these two classes of drugs, reaching 80% in 2008. The most spectacular increase in use was noted for statins, from 32.45% in 1999 to 90.43% in 2008 (Table 33, Figure 41).

Table 36 illustrates the rate of administration of the main drugs used in STEMI patients treated conservatively, with thrombolytics, or primary angioplasty. Patients with conservative treatment were significantly less often treated with anticoagulants, as compared with patients treated with thrombolytics or interventionally ($p < 0.0001$). The difference between patients treated with thrombolytics and primary angioplasty was not significant. Rates of platelet antiplatelet administration were similar in patients without reperfusion therapy, as compared with those treated with thrombolytics ($p = 0.73$), but both values were significantly lower as compared with interventionally treated patients ($p < 0.0001$).

Table 37 summarizes the utilization of adjuvant therapy in patients treated with streptokinase vs. fibrin-specific fibrinolytics. There is an ascendant gradient from streptokinase to tenecteplase, regarding the number of patients treated with heparin followed by enoxaparin; aspirin plus clopidogrel; beta-blockers; ACEIs; and statins.

Differences between patients belonging to the four groups were statistically significant comparing them in pairs from streptokinase to tenecteplase ($p < 0.0001$ for all comparisons). One explanation may be that alteplase, reteplase and tenecteplase have gradually entered use in Romania over the past decade. As shown in previous paragraphs, streptokinase utilization was gradually reduced over the past 10 years as alteplase, reteplase and tenecteplase (in that order) were introduced in current use. During the same time-frame, the rates of use of beta-blockers, ACEIs, statins and dual antiaggregation (aspirin plus clopidogrel) increased gradually. Another explanation may be a higher age of patients treated with streptokinase, an expression of more contraindications to auxiliary therapy.

III.11.3. Angiography, angioplasty, and stenting in patients treated conventionally or with thrombolytics

The global rate of angiography, angioplasty and stent deployment in RO-STEMI patients treated initially with conventional therapy or with IV thrombolytics was of 13.05%, 6.94% and 6.13%, respectively. These rates increased slowly till 2008; in 2009, the rate of angiography (27.25 %) doubled, and that of angioplasty (18.51%) and stent deployment (18.08%) trebled as compared to the previous year (12.93%, 6.45% and, 6.18%, respectively) (Table 38, Figure 45).

The rate of coronarography, angioplasty, and stent deployment was similar in patients with conservative treatment and in patients treated with thrombolytics (Table 39).

III.12. Major complications

Taking into account the differences in access to advanced technology in the different participating centers, the analysis of STEMI complications was limited to the following variables: cardiogenic shock, cardiac failure, early post-infarction angina, major hemorrhage, stroke, and early reinfarction. Table 40 shows the incidence of the different complications in those patients in whom these data were correctly recorded.

Cardiogenic shock after admission was recorded in 249 of 15017 validated patients (1.65%, probably an underestimated value). The global incidence of post-infarction heart failure was 21.50%, a value that must be critically viewed, as the diagnosis was clinically based. A group of 1506 of 14914 validated patients had post-infarction angina (10.09%), and 163 of 14808 validated patients had evidence of reinfarction (1.10%). Major hemorrhage was seen in 1.45% of validated patients.

A group of 163 out of 15053 validated patients developed stroke during hospitalization (1.08%). In 64 of these patients (0.42%), the stroke was hemorrhagic; in 39 (0.26%), it was ischemic; in 5 patients, the stroke was initially ischemic, with hemorrhagic transformation (0.003%); and in 55 patients (0.36%), the type of stroke could not be established (Table 40).

Table 41 shows the distribution of major complications in patients treated conservatively, with thrombolytics, or interventionally. There have not been significant differences among the three groups in the incidence of stroke.

As expected, the incidence of major bleeding was greatest in patients with thrombolytic therapy (2.45%), significantly higher than in patients treated conservatively (0.65%, $p < 0.0001$) and apparently unsignificantly higher as compared with interventionally treated patients (1.4%, $p =$

0.077). The difference between the incidence of major bleeding in patients with primary angioplasty and those treated conservatively was significant (p <0.0001).

Post-infarction angina was significantly more common in patients with thrombolytic treatment (13.61%), as compared with those treated conservatively (9.26%, p <0.0001) or interventionally (3.16%, p<0.0001). The difference between patients who received conservative vs. interventional therapy was also significant (p <0.0001).

Reinfarction rate was similar in patients with thrombolytic therapy (2.03%), as compared with patients treated by primary angioplasty (2.43%, p <0.613), but both values were significantly higher than the reinfarction rate in conservatively treated patients (0.31%, p <0.0001).

The incidence of major complications after myocardial infarction in patients treated with different thrombolytic agents is presented in Table 42. The overall incidence of stroke in RO-STEMI patients was 0.69% for streptokinase, 1.04% (alteplase), 0.98% (reteplase) and 2.00% (tenecteplase). Statistically, the difference between tenecteplase and streptokinase was significant, (p=0.0011), unlike that for other comparisons between subgroups. The small number of patients with hemorrhagic stroke, ischemic, hemorrhagically transformed, and cryptogenic stroke has not allowed a statistical comparison between the four thrombolytics.

The incidence of major bleeding was 1.16% (reteplase), 2.19% (alteplase), 2.62% (streptokinase) and 3.75% (tenecteplase). Differences were significant for reteplase vs. tenecteplase (p = 0.002) and reteplase vs. streptokinase (p = 0.005).

There were no significant differences between streptokinase, alteplase and reteplase in the incidence of post-infarction angina (12.99%, 15.09% and 11.44%, respectively). Apparently, the incidence of post-infarction angina was significantly decreased in patients treated with tenecteplase (7.75%, p <0.003 as compared with streptokinase, <0.0001 vs. alteplase, and 0.048 vs. reteplase). However, the fact that reinfarction was more common in patients treated with tenecteplase (3.25%) as compared with streptokinase (1.91%), alteplase (2.39%), and reteplase (1.43%) “evens out” this difference.

III.13. In-Hospital Mortality

Global mortality among the 19510 patients was 11.79%. Table 43 and Figure 46 show the global in-hospital mortality between 1997 – 2009. Of note, RO-STEMI was initially a registry for thrombolysed patients only, and only such patients are reflected for 1997 and 1998. For the same reason, the thrombolysis/ conservative ratio was greater than 1 in the 1999 – 2002 interval. However, starting in 2003, all centers have started homogeneously reporting all STEMI patients,

regardless of the therapeutic approach (Table 27 and Figure 38). Therefore, the portion of the graph subsequent to 2003 reflects best the general trend of in-hospital mortality after infarction in Romania. This mortality has progressively decreased decreased from 15.54 % in 2003 to nearly 8.39% in 2009.

Table 44 and Figure 47 present in-hospital mortality in the registry, in the interval 1997 – 2009, by Development Region. In-hospital mortality was generally between 9 and 13%.

In Region 3, reported mortality was very low (3.31%). However, this region also has the fewest patients, as many are actually transported to Bucharest, and accordingly registered in Region 8. On the other hand, in-hospital mortality was lower in regions where the mean age and the incidence of Killip class 3 or 4 on admission were lower (Table 45). This became even more obvious after the grouping of regions according to per capita GNP (Table 46, Figure 48). Mortality analysis in other patient subgroups will be the subject of separate papers.

Overall in-hospital mortality was 15.31% in patients treated conservatively, significantly higher than the 9.16% recorded in patients with thrombolytic therapy and than the 6.62% recorded in interventional patients ($p < 0.0001$ for both comparisons).

Table 47 and Figure 49 illustrate the annual in-hospital mortality in RO-STEMI patients by type of treatment (conservative therapy, thrombolysis, or primary angioplasty). A significant reduction of in-hospital mortality after 2004 is apparent both for patients treated with thrombolytic agents and for those treated by primary angioplasty. As an apparent surprise, for the last three years of follow-up mortality was virtually identical in patients treated by either of the two reperfusion procedures.

Since both fibrin-specific fibrinolytics and primary angioplasty have been used more frequently in daily practice after 2004, we performed a separate analysis of in-hospital mortality for the period 2005-2009, i.e., the last five years of follow-up, by subgroups of patients treated by different thrombolytic regimens or by primary angioplasty (Table 48 and Figure 50).

We will bear in mind here that streptokinase regimens of 0.75 M.U./10 min. 1.5 M.U./60 min. and 1.5 M.U./30 min. were given in patients of significantly higher age as compared to patients treated with fibrin-specific substances, streptokinase 1.5 MU/20 min., or primary angioplasty (Table 31). Overall hospital mortality was similar in patients treated with primary angioplasty, as compared with those treated with fibrin-specific fibrinolytics or streptokinase 1.5 M.U./20 min. or 0.75 M.U./10 min., but significantly lower than in patients who received streptokinase in slow regimens (1.5 M.U./60 min. or 1.5 M.U./30 min. $p=0.014$ and, respectively, $p < 0.0001$). For patients treated with fibrinolytics, significant differences occurred only for streptokinase 1.5 MU/30 min., as compared with reteplase ($p < 0.0001$), alteplase ($p = 0.004$) and streptokinase 1.5 MU/20

min. (p = 0.008). Similarly, significant differences emerged for subgroups of patients aged 15-74 (p = 0.003, 0.042, and, respectively, 0.011). For patients under 75, the difference was borderline significant for the comparison of streptokinase 1.5 MU/60 min. vs. streptokinase 1.5 M.U./20 min. (P = 0.050). For patients aged over 75, mortality differences were not significant for any comparison.

It is important to note here that the lack of statistical significance for some comparisons despite seemingly significant percentage differences is due, possibly, to the relatively small number of patients in the subgroups, excepting patients treated with primary angioplasty.

IV. Discussion and conclusions

IV.1. RO-STEMI-1, RO-STEMI-2 and RO-STEMI-3

In order to define the dynamics of certain variables, we have divided patients into three groups, by time of occurrence of the event, thus: 1997 - 2001 (RO-STEMI-1), 2002 - 2005 (RO-STEMI-2), and 2006-2009 (RO-STEMI-3) (Table 49).

Of note, the registry was initially (1997-1998) dedicated to thrombolysed patients only. The tendency to predominantly enroll thrombolysed patients persisted till 2001, explaining the high rate of use of this therapeutic method in the RO-STEMI 1 group, as well as the lower mean age (62 +/- 12 years) and the slightly higher proportion of (70.47%) in RO-STEMI-1 than in RO-STEMI 2 and 3 (mean age 63+/-13 years and an incidence of 67.91% and, respectively, 68.49% for the male gender). However, in RO-STEMI-2 and 3 patients, reperfusion and conservative therapy were more evenly distributed, making the comparison between these two groups more meaningful regarding the evolution of the variables over the past decade.

This analysis outlined a few interesting points. The median time between the onset of pain and hospitalization was significantly higher in RO-STEMI-3 (262 min.), as compared to RO-STEMI-2 (210 min.) and to RO-STEMI-1 (180 min.). The time difference between RO-STEMI 1 and 3 can be easily explained by the significantly higher number of thrombolysed patients in RO-STEMI-1. Although indicated within 12 hours of infarct onset, thrombolysis was preferred at the time, by our clinicians, mainly for presentations within the first 6 hours. The 52-minute difference between the median time to hospitalization in RO-STEMI 2 and 3 is not as easily explained. However, this difference is not necessarily proof later arrival in RO-STEMI 3 patients. Indeed, during the past few years, there has been a tendency to transfer patients from the initial facility to one capable of interventional therapy. This probably accounts for the fact that, in RO-STEMI-3, 10.35% of patients were admitted in the interval of 12-24 hours of symptom onset, and 16.39% after 24 hours, as compared to only 7.83% and, respectively, 11.64% of RO-STEMI-2 patients ($p < 0.0001$) (Table 50 and Figure 51). This explanation is further supported by the significant increase, after 2006, of the number of patients who, after initial thrombolytic or conservative therapy, underwent angiography, angioplasty, and stent deployment (Tables 38, 39 and Figure 45).

Over the 13 years of observation, there has been a trend towards an increase in the incidence of hypertension, diabetes, smoking, obesity, and dyslipidemia. The differences between RO-STEMI-

2 and 3 patients were statistically significant (p=0.034 for hypertension and < 0.0001 for dyslipidemia and diabetes). The differences between RO-STEMI 2 or 3 on one hand, and RO-STEMI 1 on the other hand, were also significant (p < 0.0001 for all 3 variables). Conversely, there was a significant reduction in the number of smokers between RO-STEMI-3 and RO-STEMI 2 (p < 0.0001) (Table 49).

Comparative analysis of the three time intervals underscored the gradual adaptation of physicians in Romania to the guidelines for myocardial infarction published during the last decade, a fact supported by the strongly significant increase in utilization of ACE-inhibitors, beta-blockers, and statins, as well as of the combinations between Aspirin and Clopidogrel, with a constant gradient between RO-STEMI-1 and RO-STEMI-3 (Table 49).

There was an important increase of the use of primary angioplasty in STEMI. Thus, while in RO-STEMI-1 no patient had primary angioplasty, 7.45% of RO-STEMI-2 patients and 18.08% of RO-STEMI-3 patients were thus treated. The same positive evolution of interventional therapy was noted in patients under conservative or thrombolytic therapy, with an ever stronger gradient from RO-STEMI-1 to RO-STEMI-3 (p < 0.001 for all comparisons between the 3 groups) (Table 49).

All these therapeutical gains, registered in the past decade, explain the progressive reduction of in-hospital mortality by almost 4% between RO-STEMI-3 (10,83%) and RO-STEMI-2 patients (13,73%, p < 0.0001).

IV.2. Comparisons between RO-STEMI and international registries

What is the place of RO-STEMI in the international STEMI context of the past decade? We tried to answer by comparing RO-STEMI data with those of three international registries published in this period: the Euro Heart Survey – Acute Coronary Syndrome (EHS-ACS) 1 and 2 and EHS-ACS SNAPSHOT (16) (17) (18). EHS-1-ACS has enrolled, between September 2000-May 2001, a total of 4431 patients from 103 centers in 25 countries (16). EHS-ACS-2 has enrolled 3004 patients hospitalized in 2004 in 190 centers in 32 countries (17).

SNAPSHOT was a “flash” registry, which enrolled 4343 patients with acute myocardial infarction with or without ST elevation admitted between 7 -13 December 2009 in 485 centers in 47 member countries of the European Society of Cardiology. Of these, 3209 were enrolled directly into the central database, 828 were taken from the MINAP registry (England + Wales) and 306 from the Swedish registry. MINAP patients and Swedish registry patients had been hospitalized between 7-13 December 2009. By virtue of its 271 patients enrolled in this registry, Romania ranked third of the 47 participating countries. Basically, Romania enrolled in SNAPSHOT all patients with myocardial infarction admitted to hospitals in our country between 7-13 December 13, 2009. Of the 4343 patients enrolled in SNAPSHOT, 2312 had ST elevation (1871 were directly introduced into the central database, 329 were taken from MINAP, and 112, from the Swedish register) (18).

For comparison purposes, we have extracted from the RO-STEMI registry those patients admitted in the years of the international registries: 2000-2001 (for RO-STEMI-1), 2004 (RO-STEMI -2) and 2009 (RO-STEMI -3). Comparative data are presented in Table 51. It is important to remind here that in 2000-2001 RO-STEMI predominantly enrolled patients treated with thrombolytics. For this reason, the fact that 63% of RO-STEMI patients were treated with thrombolytics, and that the onset-to-admission time was of only 180 minutes should not be considered as "better" than the results recorded in EHS-ACS-1 in the same period. For the same reason, a more truthful comparison can be found in assessing RO-STEMI-2004 and EHS-ACS-2 , or RO-STEMI-2009 and SNAPSHOT.

The mean age of RO-STEMI patients was similar to that recorded in other registries. The percentage of females was consistently higher in STEMI than in other registries, the differences being statistically significant for comparisons referring to the years 2004 and 2009 ($p < 0.0001$).

The number of hypertensive patients progresively increased both in RO-STEMI and in the other three registries. The difference was significantly higher in regard to SNAPSHOT-2009 (60.0%) vs. RO-STEMI-2009 (55.83%). The percentage of smokers decreased slightly (but significantly) in RO-STEMI (from 49-50% in 2000-2001 and 2004 to 46% in 2009). However, the decrease in the number of smokers was significantly higher in the three EHS registries, from 63% in 2000-2001 to 45% in 2004 and 39% in 2009 (Table 40). In contrast, the incidence of dyslipidaemia in patients with myocardial infarction with ST-segment elevation had an opposite trend in RO-STEMI as compared to EHS registries. Thus, if the RO-STEMI incidence of dyslipidemia increased progressively from 34.5% (2000-2001) to 43.2% (2004) and 45.9% in 2009, in EHS registries it has declined from 46.8% (2000-2001) to 43.2% (2004) and 40% in 2009. The incidence of diabetes was virtually identical (21-22%) in all registries.

The onset-to-admission time appeared to increase in RO-STEMI (from a median of 220 minutes in 2004 to 255 minutes in 2009), and has decreased in EHS records from 210 minutes (EHS-ACS -1) to 170 minutes (EHS-ACS-2). This time is not available for SNAPSHOT.

Apart from the data in RO-STEMI-1, there was an increase in the number of patients with reperfusion therapy, from 46.09% in 2004 to 53.59% in 2009. However, these values were significantly lower than those of 63.99% and 70% recorded in EHS-ACS for the same years. The greatest differences between RO-STEMI and EHS-ACS registries appear when comparing rates of use of primary angioplasty as a means of reperfusion. Thus, no RO-STEMI patient underwent this procedure in 2000-2001, as compared to 20.71% of patients in EHS-ACS-1. In 2004, the ratio was 7.73% (RO-STEMI) vs. 37.76% (EHS-ACS-1). For 2009, the ratio decreased: 31.40% vs. 50.00%. A progressive increase in the number of patients treated by primary angioplasty led to a progressive reduction of patients treated with thrombolytics (Table 51).

Interestingly, the number of patients who received anticoagulants appeared to be higher in RO-STEMI 1 and 2 patients, as compared with those in EHS-ACS 1 and 2. Antiplatelet agent utilization

in RO-STEMI patients appeared similar to that recorded in EHS-ACS patients. This was due to aspirin use in almost all STEMI patients. Conversely, utilization of dual antiaggregation (aspirin plus clopidogrel), progressively increasing in all registries, was consistently significantly higher in EHS-ACS patients (in 2009, 65.69% for RO-STEMI vs. 94% for SNAPSHOT).

Data presented in this report showed a gradual increase in the use of ACE inhibitors, beta-blockers, and statins in RO-STEMI patients. However, as can be seen from Table 51, utilization rates were consistently significantly lower than the EHS-ACS rates. An exception occurs regarding the percentage of patients treated with angiotensin enzyme inhibitors in RO-STEMI-1 (71%), as compared with EHS-ACS-1 (62%).

Although the percentage of RO-STEMI patients treated initially with thrombolytic therapy or conservatively, with subsequent coronary angiography, has increased progressively (from 3.97% in 2000-2001 to 14.76% in 2004 and to 34.23% in 2009), it remains far from EHS-ACS results (58.10% in 2000-2001, 70.20% in 2004 and 51.00% in 2009).

Overall mortality appeared to decrease in RO-STEMI patients from 13.21% in 2004 to 8.39% in 2009, while in EHS-ACS patients it remained constant (7.0% in 2000 - 2001, 6.40% in 2004 and 8.5% in 2009). The important parameter, however, is in-hospital RO-STEMI mortality irrespective of therapy. Thus, mortality in conservatively treated patients was reduced from 16.91% in 2004 to 11.72% in 2009. For patients treated with thrombolytics, in-hospital mortality was 8.98% (in 2000-2001), 7.94% (2004) and 5.29% (in 2009), and for those treated by primary angioplasty mortality was 9.14% in 2004 and 5.52% in 2009. Thus, while overall in-hospital mortality was higher in RO-STEMI 1 and 2 as compared to EHS-ACS 1 and 2, this was almost similar in 2009 for RO-STEMI-3 as compared to SNAPSHOT. While in-hospital mortality in patients treated with conservative therapy or primary angioplasty is similar in RO-STEMI-3 and SNAPSHOT, RO-STEMI patient mortality under thrombolytic therapy is significantly lower than in SNAPSHOT (Table 51).

A more accurate picture of Romania's situation in 2009 in terms of STEMI patient characteristics, modalities of treatment and hospital course can be outlined by comparing RO-STEMI-2009 data to for the same year, by grouping the participating countries in four regions: North, West, Central and Eastern Europe and the Mediterranean countries (Figure 52) (18). The data presented in Table 41 are, we think, conclusive.

Thus, RO-STEMI patient age (63.33 + / -12 years) is similar to that of patients in Central and Eastern European countries, and in the middle of the mean age values recorded in the Mediterranean region (62 years) and in Northern and Western countries (64 years). The 30% prevalence of female gender is close to that of 33% in Central and Eastern Europe but higher than that recorded in the North and the West.

The incidence of hypertension was significantly higher in SNAPSHOT patients from Central and Eastern Europe (66%). The incidence of hypertension in RO-STEMI -2009 (55.83%) patients was

similar to that recorded in patients from Mediterranean and Western, but significantly higher than that recorded in patients from the Nordic countries. The incidence of smoking and dyslipidemia was higher in RO-STEMI patients, as compared to that recorded in patients from the four geographical regions. A 23% incidence of diabetes was comparable to the 25% reported in Mediterranean countries, but significantly higher than that recorded in patients from Northern or Western countries.

The proportion of patients who had a history of MI was lowest in Romanian patients, as compared with patients reported by the four regions. This finding raises the suspicion of a higher survival rate in patients of previous infarctions in the four geographical regions. The same suspicion occurs when we find that the percentage of RO-STEMI patients admitted with Killip class III or IV (13.80%) was lower than that of patients from the four geographical regions.

The proportion of RO-STEMI-2009 patients treated by reperfusion therapy was very close to that of patients in the Northern countries, but clearly lower than that reported for the other three geographic regions. Conversely, the number of Romanian patients treated by primary angioplasty was significantly lower, as compared with that in the four regions. Onset-to-admission time was significantly longer for Romanian patients, as compared to each of the four geographical regions.

In patients treated with thrombolytics or conservatively, coronary angiography was performed in a similar proportion of RO-STEMI – 2009 and other Central and Eastern European patients, but this proportion was clearly lower than that reported for the Northern, Western, or Mediterranean countries.

The proportion of RO-STEMI-2009 patients treated with dual antiplatelet therapy, beta-blockers or statins was significantly lower than in the four geographical regions. The same observation can be made in respect of the rate of ACE inhibitor administration, excepting a higher value for RO-STEMI-2009, as compared with the Northern countries.

The overall mortality of RO-STEMI-2009 patients appeared slightly lower than in other Central and Eastern European countries; similar to the Mediterranean countries; but higher than that of Northern or Western countries.

V. Limitations

The limitations of RO-STEMI are important. Firstly, the number of participating centers has varied along the registry duration. On the one hand, this number has gradually increased but, on the other hand, some centers have not had a constant annual reporting. The data in the registry could not be validated for all included patients, given the occasional absence of information. However, for each variable, data validation was usually possible in over 80-90% of patients, preventing significant distortion of the results. A balanced geographical distribution of the centers and participation of both traditional and newer academic centers, such as county, municipal, or city hospitals are strong reasons to consider the data as a truthful reflection of the STEMI reality in Romania, during the first decade of the 21st century.

Apendix 1. Annual RO-STEMI data centralization

Valentin Chioncel, MD (1997), Aurelia Bumbu, MD (1998), Alexandrina Tatu-Chitoiu, MD (1999), Cristina Teodorescu, MD (2000), Alexandra Diaconeasa, MD (2001), Elvira Craiu, MD, PhD (2002), Luminita Serban, MD, and Raluca Jumatate, MD (2003), Calin Pop, MD, PhD (2004), Dragos Vinereanu, MD, PhD, and Vlad Vintila, MD (2005), Antoniu Petris, MD (2006), Diana Tint, MD (2007), Gabriel Tatu-Chitoiu, MD (2008, 2009)

Table 1. RO-STEMI Centers and their annual contribution to the Register

No.	CENTRE	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	TOTAL
1	"Floreasca" Emergency Clinical Hospital, Bucharest	131	174	168	296	268	151	456	426	348	377	314	306	263	3678
2	Emergency Municipal Hospital, Roman	3	2	11	6	9	10	5	11	4	36	43	45	46	231
3	Emergency County Hospital, Braila	11	23	21	35	32	22	18	38	40	21	5	34	49	349
4	Emergency Clinical County Hospital, Constanta			35	72	45	65	40	86	91	118	232	158	236	1178
5	"Sf. Pantelimon" Emergency Clinical Hospital, Bucharest			26	75	45	86	61	84	26	176	0	0	0	579
6	Municipal Hospital, Timisoara			106	102	126	97	105	72	60	97	9	25	18	817
7	"Bagdasar-Arseni" Emergency Clinical Hospital, Bucharest				75	109	121	137	151	79	261	113	129	136	1311
8	"Prof. Dr.C.C. Iliescu" Emergency Institute of Cardiovascular Diseases, Bucharest				2	1	4	3	13	1	0	0	109	169	302
9	Emergency University Hospital, Bucharest				37	89	98	91	156	0	334	0	0	59	864
10	Emergency Clinical County Hospital, Brasov			7	133	1	0	0	150	40	178	0	187	51	747
11	Emergency Clinical County Hospital, Sibiu						117	113	115	124	165	19	285	23	961
12	Institute of Cardiovascular Diseases, Timisoara								94	70	137	5	0	78	384
13	Cardiology Center, Craiova								66	46	84	166	148	43	553

No.	CENTRE	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	TOTAL
14	Emergency Clinical County Hospital, Oradea								251	0	73	0	315	29	668
15	Emergency County Hospital, Ramnicu Valcea								18	0	27	87	12	0	144
16	Emergency County Hospital, Targoviste								1	51	67	90	81	15	305
17	„Sf.I Spiridon" Emergency Clinical County Hospital, 1st Medical Clinic, Iasi									20	102	101	46	76	345
18	Emergency County Hospital, Slatina									1	17	0	0	0	18
19	Emergency Clinical County Hospital, Arad										146	184	172	0	502
20	"Prof. Dr. George I.M. Georgescu" Institute of Cardiovascular Diseases, Iasi										106	86	97	83	372
21	Colentina Emergency Clinical Hospital, Bucharest										20	3	0	11	34
22	"Sf. Apostol Andrei" Emergency Clinical Hospital, Galati										52	0	12	65	129
23	Emergency Clinical County Hospital, Cluj-Napoca										97	0	0	101	198
24	„Sfintii Doctori Fara de Arginti Cosma si Damian" Hospital, Radautii										41	5	46	54	146
25	Emergency County Hospital, Pitesti										108	1	22	0	131
26	City Hospital, Campia Turzii										1	9	0	0	10
27	Emergency Clinical Hospital "Sf. Ioan"										2	15	0	0	17
28	Emergency County Hospital, Baia Mare											113	95	99	307
29	Municipal Hospital, Fagaras											11	0	0	11
30	Cardiovascular Diseases Emergency Clinical Center of the Army, Bucharest											9	34	26	69
31	Caritas Clinical Hospital "Acad. Prof. Dr. N. Cajal" Bucharest											41	10	34	85
32	"Elias" Emergency University Hospital, Bucharest											6	0	0	6
33	Emergency Clinical County Hospital, Ilfov											2	0	13	15
34	Emergency County Hospital, Satu Mare											2	0	0	2
35	"Dr. Fogolyan Kristof" Emergency County Hospital, Sfantu Gheorghe											40	39	13	92
36	Emergency County Hospital, Targu Jiu											32	0	0	32

No.	CENTRE	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	TOTAL
37	"Ion Jianu" Emergency Military Hospital, Pitesti											1	0	0	1
38	Municipal Hospital, Targu Neamt											27	0	28	55
39	Municipal Hospital, Sighetul Marmatiei												10	4	14
40	Emergency County Hospital Targu Mures (Regional registry of myocardial)								390	331	339	390	263	226	1939
41	Institute of Cardiology and Heart Transplant, Targu Mures												5	201	206
42	"Prof. Dr. Niculae Stancioiu" Heart Institute, Cluj Napoca								141	174	198	224	332	433	1502
43	ICCO Clinics, Brasov													201	201
	TOTAL	145	199	374	833	725	771	1029	2263	1506	3380	2385	3017	2883	19510

Table 2. Types of Centers participating in RO-STEMI

No.	Traditional University Hospitals
1	The Cardiology Centre Craiova
2	The Institute for Cardiovascular Disease "Prof. Dr. George I. M. Georgescu" Iasi
3	The Institute for Cardiovascular Disease Timisoara
4	The Institute for Cardiology And Cardiac Transplant Targu Mures
5	The Emergency Institute Cardiovascular Disease "Prof. Dr. C. C. Iliescu" Bucharest
6	The Heart Institute "Prof. Dr. Niculae Stancioiu" Cluj - Napoca
7	The Clinical Hospital Caritas "Acad. Prof. Dr. N. Cajal" Bucharest
8	The Clinical Emergency Hospital "Bagdasar-Arseni Bucharest"
9	The Clinical Emergency Hospital "Floreasca" Bucharest
10	The Clinical Emergency Hospital "Sf. Ioan"
11	The Clinical Emergency Hospital "Sfantul Pantelimon" Bucharest
12	The County Emergency Clinical Hospital Cluj-Napoca
13	The County Emergency Clinical Hospital "Sf. Spiridon" - Ist Medical Cardiology Clinic Iasi
14	The University Clinical Hospital Colentina Bucharest
15	The County Hospital Targu Mures
16	The Municipal Hospital Timisoara
17	The University Emergency Hospital of the City of Bucharest
18	The Elias University Emergency Hospital Bucharest
No.	**County Hospitals (some of which subsequently became University Hospitals)**
1	The Clinical Emergency Hospital "Sf. Apostol Andrei" Galati
2	The Clinical Emergency Hospital Oradea *
3	The County Emergency Clinical Hospital Arad
4	The County Emergency Clinical Hospital Brasov *
5	The County Emergency Clinical Hospital Constanta *

Table 2 – cont.

No.	County Hospitals (some of which subsequently became University Hospitals)
6	The County Emergency Clinical Hospital Ilfov
7	The County Emergency Clinical Hospital Sibiu*
8	The County Emergency Hospital "Dr. Fogolyan Kristof" Sfantu Gheorghe
9	The County Emergency Hospital Baia Mare
10	The County Emergency Hospital Braila
11	The County Emergency Hospital Pitesti*
12	The County Emergency Hospital Râmnicu Valcea
13	The County Emergency Hospital Satu Mare
14	The County Emergency Hospital Slatina
15	The County Emergency Hospital Targoviste
16	The County Emergency Hospital Targu Jiu
No.	**Municipal or City Hospitals**
1	The "Sfintii Doctori Fara de Arginti Cosma And Damian" Hospital Radauti
2	The Municipal Emergency Hospital Roman
3	The Municipal Hospital Fagaras
4	The Municipal Hospital Sighetul Marmatiei
5	The Municipal Hospital Targu Neamt
6	The Campia Turzii City Hospital
No.	**Military Hospitals**
1	The Army Emergency Centre for Cardiovascular Disease Bucharest
2	The Emergency Military Hospital "Ion Jianu" Pitesti
No.	**Private Hospitals**
1	The ICCO Clinics Brasov

Table 3. Key Indicators for Regional Development in Romania

Region	Population*	GNP/capita (Euro) 2005**	Urban population (%) 2005**	B and C ambulances /100.000 inhabitants*	Hospital day care facilities 2005*	Number of hospitals 2007*	Angiography facilities 2004
North-East	3 734 546	2029.3	43,4	1,26	45	67	2
South-East	2 846 379	2661.35	55,5	2,24	41	47	1
South	3 329 762	2447	41,7	2,21	47	62	0
South-West	2 306 450	2443.9	47,5	1,77	36	42	1
West	1 930 458	3363.7	63,6	2,44	21	46	2
North-West	2 737 400	2850.7	53,1	2,61	34	62	4
Centre	2 530 486	3056.9	59,8	4,30	39	51	4
Bucharest-Ilfov	2 208 368	5616.7	90,5	2,70	33	59	11

*Source: *Ministry of Public Health, 2005; **Romania's Statistical Record 1999, 2006.*
Ambulance Type C = Resuscitation And Intensive Care Ambulance - ARTI (type C); Ambulance Type B = Emergency And Resuscitation – AUR (type B); Ambulance Types A_1 And A_2 = Ambulance For Assisted Transport ATA – A_1 For One Patient. A_2 For More Than One Patient; Ambulance AT= Ambulance For Transport And House Calls For One Or More Patients – AT_1, AT_2.

Table 4. Data Sources for RO-STEMI

No.	Source	No. patients	%
1	RO-STEMI central database	15483	79.35
2	Regional Infarction Registry Tg. Mures (2004-2009)	1939	9.93
3	Heart Institute Cluj-Napoca (2004-2009)	1502	7.69
4	County Hospital Oradea (2008)	315	1.61
5	Sibiu County Hospital (2008)	271	1.38
	TOTAL	**19510**	**100**

Table 5. RO-STEMI Patient Distribution by Type of Hospital

Type of hospital	Traditional university	County	Municipal/ City	Military	Private	TOTAL
Patients	13193	5578	466	70	201	19510
%	*67.61*	*28.95*	*2.39*	*0.35*	*1.03*	*100.00*

Table 6. RO-STEMI Patient Distribution by Development Region

Region	1	2	3	4	5	6	7	8	TOTAL
Patients	1149	1656	452	747	1703	2701	4157	6945	19510
%	*5.88%*	*8.48%*	*2.31%*	*3.82%*	*8.72%*	*13.84%*	*21.30%*	*35.59%*	*100.00%*

Table 7. Annually Enrolled Patients in the RO-STEMI Registry by Development Region

Region	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	TOTAL
1	3	2	11	6	9	10	5	11	24	285	262	234	287	1149
2	11	23	56	107	77	87	58	124	131	191	237	204	350	1656
3	0	0	0	0	0	0	0	1	51	175	94	103	28	452
4	0	0	0	0	0	0	0	84	47	128	285	160	43	747
5	0	0	106	102	126	97	105	166	130	380	198	197	96	1703
6	0	0	0	0	0	0	0	392	174	369	348	752	666	2701
7	0	0	7	133	1	117	113	655	495	682	460	779	715	4157
8	131	174	194	485	512	460	748	830	454	1170	501	588	698	6945
TOTAL	**145**	**199**	**374**	**833**	**725**	**771**	**1029**	**2263**	**1506**	**3380**	**2385**	**3017**	**2883**	**19510**

Table 8. Distribution of 14145 RO-STEMI Patients by Admission Month

Month	Jan	Feb	Mar	Apr	May	June	July	Aug	Sep	Oct	Nov	Dec	TOTAL
Patients	1244	1204	1360	1283	1330	1179	1012	992	1023	1249	1105	1164	14145
%	*8.79%*	*8.51%*	*9.61%*	*9.07%*	*9.40%*	*8.33%*	*7.15%*	*7.01%*	*7.23%*	*8.83%*	*7.81%*	*8.22%*	*100%*

Table 9. Circadian Distribution of STEMI Onset in 11743 RO-STEMI Patients

Hours	0:00-03:59	04:00-07:59	08:00-11:59	12:00-15:59	16:00-19:59	20:00-23:59	TOTAL
Patients	1860	1992	1787	2345	1952	1807	11743
%	*15.83*	*16.96*	*23.73*	*19.96*	*16.62*	*15.38*	*100*

Table 10. Circadian Distribution of Admission Time in 11408 RO-STEMI Patients

Hours	0:00-03:59	04:00-07:59	08:00-11:59	12:00-15:59	16:00-19:59	20:00-23:59	TOTAL
Patients	1227	1114	2548	2728	2044	1747	11408
%	*10.75*	*9.76*	*22.35*	*23.91*	*17.91*	*15.31*	*100*

Table 11 . Distribution of 10907 RO-STEMI Patients by Transport Modality to the Hospital

(Pub. Tr. = Public transportation; Hosp. = Patient hospitalized prior to STEMI onset)

Type	Ambulance	Own	Pub. Tr.	On Foot	Police	Hosp.	TOTAL
Patients	9141	1638	14	6	2	106	10907
%	*83.80%*	*15.01%*	*0.10%*	*0.05%*	*0.02%*	*0.97%*	*100%*

Table 12. Distribution of 8701 Male and 3778 Female RO-STEMI Patients by Pain Onset-to-admission Time

Time (hours)	0-3	3-6	6-12	12-24	24-48	48-72	72-96	96-120	120-144	144-168	> 7 days	Total
Male	3476	2313	1137	713	426	263	201	56	42	9	65	8701
%	*39.95*	*26.58*	*13.06*	*8.19*	*4.89*	*3.02*	*2.31*	*0.64*	*0.48*	*0.1*	*0.74*	*100*
Female	1104	1072	608	402	193	148	146	45	13	5	42	3778
%	*29.22*	*28.37*	*16.09*	*10.64*	*4.1*	*3.97*	*3.86*	*1.19*	*0.34*	*0.13*	*1.11*	*100*
Total	4580	3385	1745	1115	619	411	347	101	55	14	107	12479
%	*36.69*	*27.12*	*13.98*	*9.21*	*4.95*	*3.31*	*2.78*	*0.8*	*0.44*	*0.11*	*0.8*	*100*

Table 13. Distribution of 12479 RO-STEMI Patients by Age Group and Pain-to-admission Time

Pain-to-admission time/age	< 45	45-59	60-74	>75	TOTAL
0-179 min.	507	1866	1615	591	4579
%	45.13%	43.75%	33.68%	25.72%	36.69%
180-359 min.	291	1137	1334	624	3386
%	25.95%	26.65%	27.82%	27.16%	27.13%
360-719 min.	126	506	738	375	1745
%	11.23%	11.86%	15.39%	16.32%	13.98%
720-1439 min.	93	319	442	256	1110
%	8.29%	7.47%	9.21%	11.14%	8.89%
>24 hours	106	437	665	451	1659
%	9.45%	10.24%	13.87%	19.63%	13.29%
TOTAL	**1122**	**4265**	**4794**	**2297**	**12479**

Table 14. Distribution of 12063 RO-STEMI Patients by Gender and Admission-to-treatment Onset Time

Time (min.)	0-29	30-59	60-89	90-119	120-179	> 180	Total
Males	3956	3525	568	176	91	106	**8422**
%	*46.97%*	*41.85%*	*6.74%*	*2.09%*	*1.08%*	*1.25%*	***100.00%***
Females	1530	1673	243	85	52	58	**3641**
%	*42.02%*	*45.94%*	*6.67%*	*2.33%*	*1.42%*	*1.59%*	***100.00%***
TOTAL	**5486**	**5198**	**811**	**261**	**143**	**164**	**12063**
%	*45.47%*	*43.09%*	*6.72%*	*2.16%*	*1.18%*	*1.36%*	***100.00%***

Table 15. Distribution of 12063 RO-STEMI Patients by Age Group and Admission-to-treatment Onset Time

Age	< 45	45-59	60-74	>75	TOTAL
0 - 29 min.	555	1948	2032	951	5486
%	*51.15%*	*47.25%*	*43.86%*	*42.70%*	*45.47%*
30 - 59 min.	406	1680	2067	1045	5198
%	*37.41%*	*40.75%*	*44.62%*	*46.98%*	*43.09%*
60 - 89 min.	59	302	321	129	811
%	*5.43%*	*7.32%*	*6.93%*	*6.72%*	*6.72%*
90 - 119 min.	32	90	95	44	261
%	*2.94%*	*2.18%*	*2.05%*	*1.97%*	*2.16%*
120 - 179 min.	14	47	53	29	143
%	*1.29%*	*1.14%*	*1.14%*	*1.30%*	*1.18%*
> 180 min.	19	55	64	26	164
%	*1.75%*	*1.33%*	*1.38%*	*1.17%*	*1.36%*
TOTAL	**1085**	**4122**	**4632**	**2224**	**12063**

Table 16. Distribution by Gender and Mean Age in RO-STEMI Patients

	Males	Females	TOTAL
Patients	13376	6134	19510
%	*68.56*	*31.44*	*100*
Age	60.92+/-12	67.43+/-12	63.39+/-12

Table 17. Distribution by Age Group and of RO-STEMI Patients

Age	Males	%	Females	%	TOTAL	%
15 - 19	6	*0.003*	0	*0.003*	6	*0.003*
20 - 24	15	*0.008*	3	*0.002*	18	*0.103*
25 - 29	58	*0.33*	6	*0.003*	64	*0.367*
30 - 34	154	*0.88*	20	*0.11*	174	*0.998*
35 - 39	390	*2.23*	42	*0.24*	432	*2.479*
40 - 44	651	*3.73*	109	*0.62*	760	*4.362*
45 - 49	1208	*6.93*	228	*1.308*	1436	*8.242*
50 - 54	1507	*8.649*	329	*1.884*	1836	*10.538*

Table 17 – cont.

Age	Males	%	Females	%	TOTAL	%
55 - 59	1746	*10.021*	454	*2.605*	2200	*12.677*
60 - 64	1494	*8.575*	571	*3.277*	2065	*11.852*
65 - 69	1695	*9.729*	1002	*5.751*	2697	*15.48*
70 - 74	1403	*8.53*	983	*5.642*	2386	*13.695*
75 - 79	965	*5.538*	932	*5.349*	1897	*10.888*
80 - 84	476	*2.732*	554	*3.179*	1030	*5.912*
85 - 89	137	*0.786*	209	*1.199*	346	*1.985*
90 - 94	27	*1.549*	47	*0.269*	74	*0.424*
> 95	0	*0*	1	*0*	1	*0*
TOTAL	**11932**	***70.22***	**5490**	***29.78***	**17422**	***100***
Mean	**60.92+/-12**	/	**67.43+/-12**	/	**63.39+/-12**	/

Table 18. Mean Age in RO-STEMI Patients in the Interval 1997-2009

	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	Global
Males	*56.95*	*57.19*	*58.22*	*59.63*	*59.6*	*59.23*	*60.25*	*59.73*	*59.36*	*60.02*	*60.58*	*60.06*	*59.36*	*59.74*
SD	11.72	11.7	12.09	11.6	11.3	12.05	12.55	12.01	12.86	12.96	12.53	12.81	12.79	12.5
Median	59	57	59	60	60	60	60	59	58	59	60	59	59	59
Females	*68.68*	*67.05*	*66.6*	*66.53*	*68.62*	*67.47*	*67.92*	*67.07*	*68.38*	*68.89*	*68.41*	*68.07*	*68.27*	*68.07*
SD	10.42	10.62	10.43	11.66	9.85	11.22	11.48	11.41	12	11.67	11.2	12.02	11.88	11.52
Median	69	70	67	67	70	69	70	69	70	71	69	71	70	70
Global	*60.27*	*59.91*	*60.86*	*61.61*	*62.33*	*62*	*62.68*	*61.97*	*62.29*	*62.92*	*62.96*	*62.53*	*61.98*	*62.32*
SD	12.51	12.21	12.22	12.02	11.64	12.4	12.72	12.3	13.27	13.22	12.66	13.1	13.17	12.8
Median	62	60	61	63	63	64	64	63	63	64	64	63	62	63

Table 19. Development Region and Mean Age in RO-STEMI Patients

Region	1	2	3	4	5	6	7	8	Global
Males	61.08+/-13.28	57.34+/-11.9	59.15+/-12.5	59.17+/-12.4	60.68+/-11.7	61.08+/-12.09	61.22+/-12.0	59.76+/-12.7	59.74+/-12.5
Females	68.29+/-12	65.67+/-11.9	67.83+/-11.0	67.18+/-9.7	67.53+/-10.7	67.94+/-11.6	67.67+/-11.8	69.13+/-11.7	68.07+/-11.5
Global	63.34+/-13.3	59.61+/-12.5	61.68+/-12.6	61.36+/-12.3	62.91+/-11.8	63.48+/-12.4	62.92+/-12.7	62.63+/-13.1	62.32+/-12.8

Table 20. Distribution of RO-STEMI Patients by Development Region, Grouped as Follows: Regions 1,2,3 and 4 (Regions with a GNP per Capita under 2800 Euro); Regions 4,5 and 6 (Regions with a GNP per Capita between 2800 and 5600 Euro); Region 8 (GNP per Capita over 5600 Euro)

	Regions 1,2,3,4		Regions 5,6,7		Region 8		TOTAL	
	No.	%	No.	%	No.	%	No.	%
Males	2862	*71.47*	5291	*66.34*	4822	*69.43*	12945	*68.4*
Age (n+/-SD)	*59.00+/-12*	/	*61.34+/-11.5*	/	*60.00+/-13*	/	*60.0+/-13.0*	/
Females	1142	*28.53*	2684	*33.65*	2123	*30.56*	5949	*31.43*
Age (n+/-SD)	*67.00+/-11*	/	*67.6+/-10.19*	/	*69.00+/-12*	/	*68.0+/-12.0*	/
Total	4004	*100*	7975	*100*	6945	*100*	18924	
Age (n+/-SD)	*61.00+/-13*	/	*63.71+/-11.9*	/	*62.00+/-13*	/	*62.0+/-13.0*	/

Table 21. Incidence of the Maincoronary Risk Factors in RO-STEMI Patients

Patients	HTN	Smoking	Dyslipidaemia	Diabetes	Old MI	Obesity
N/Validated	9585/18304	8573/18216	7011/17819	3998/18234	1495/18971	3235/14672
%	*52.36%*	*47.06%*	*39.34%*	*21.92%*	*7.88%*	*22.04%*

Table 22. Incidence of the Main Coronary Risk Factors in RO-STEMI Patients in the Interval 1997-2009

	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009
HTN	47/144	9/199	135/374	391/833	377/725	410/771	561/1029	1096/2121	699/1330	1764/3181	1114/2152	1003/1828	1175/2114
%	*32.63%*	*45.50%*	*36.10%*	*46.69%*	*52.00%*	*53.20%*	*54.50%*	*51.62%*	*52.56%*	*55.46%*	*51.77%*	*54.90%*	*55.60%*
Smoking	9/144	14/199	145/374	428/833	358/725	400/771	543/1029	1046/2122	594/1330	1542/3181	887/2096	812/1831	908/2078
%	*63.00%*	*70.00%*	*38.80%*	*51.40%*	*49.40%*	*51.90%*	*52.80%*	*49.30%*	*44.67%*	*48.48%*	*42.32%*	*44.30%*	*43.70%*
Dyslipidaemia	2/144	5/199	69/374	271/833	266/722	230/771	461/1029	779/2115	488/1318	1347/3175	688/1888	684/1639	935/2109
%	*14.00%*	*25.00%*	*18.40%*	*32.50%*	*36.80%*	*29.80%*	*44.80%*	*36.84%*	*37.03%*	*42.43%*	*36.44%*	*41.73%*	*44.30%*
Diabetes	1\144	7/199	54/374	153/833	177/725	175/771	182/1029	448/2121	270/1330	728/3181	450/2117	446/1793	491/2117
%	*7.00%*	*35.00%*	*14.40%*	*18.40%*	*24.40%*	*22.70%*	*17.70%*	*21.13%*	*20.30%*	*22.89%*	*21.26%*	*24.90%*	*23.20%*
Obesity	6/114	4/199	63/374	169/833	183/725	142/771	176/1029	418/1732	222/1000	749/2839	287/1499	358/1605	458/1921
%	*42.00%*	*20.00%*	*16.80%*	*20.30%*	*25.20%*	*18.40%*	*17.10%*	*24.10%*	*22.20%*	*26.40%*	*19.10%*	*22.30%*	*23.80%*
Old MI	2/145	14/199	40/351	95/763	59/681	47/691	79/971	175/1654	98/999	279/2842	158/1598	163/1558	208/2071
%	*1.40%*	*7.00%*	*11.40%*	*12.50%*	*8.70%*	*6.80%*	*8.10%*	*10.60%*	*9.80%*	*9.80%*	*9.90%*	*10.50%*	*10.00%*

Table 23. Incidence of the Main Risk Factors in RO-STEMI Patients by Age Group

	HTN	%	Smoking	%	Dyslipidaemia	%	Diabetes	%	Obesity	%	Old MI	%
< 25	3/23	*13.04%*	13/23	*56.50%*	1/23	*4.30%*	2/23	*8.70%*	2/23	*8.69%*	1/21	*4.76%*
25 -29	10/60	*16.66%*	46/60	*76.70%*	17/58	*29.30%*	2/50	*3.30%*	13/58	*22.40%*	2/56	*3.60%*
30-34	28/161	*17.39%*	124 /161	*77.00%*	66/156	*42.30%*	13/161	*8.10%*	43/156	*27.60%*	11/152	*7.20%*
35-39	96/377	*25.50%*	294/ 376	*78.20%*	150/363	*41.30%*	27/374	*7.20%*	86/355	*24.20%*	15/362	*4.10%*
40-44	234 / 694	*33.70%*	520/694	*74.90%*	299/678	*44.10%*	83/690	*12.00%*	168/671	*25.00%*	42/650	*6.50%*
45-49	554 / 1308	*42.40%*	925/1304	*70.90%*	574/1273	*45.10%*	229*/1300	*17.60%*	301/1253	*24.00%*	98/1231	*8.00%*
50-54	880 / 1819	*48.40%*	1223/1813	*67.50%*	826/1761	*46.90%*	346/1808	*19.10%*	466/1729	*27.00%*	167/1729	*9.70%*
55-59	1058 /1973	*53.60%*	1162/1958	*59.30%*	820/1901	*43.10%*	481/1964	*24.50%*	470/1871	*25.10%*	163/1864	*8.70%*
60-64	1010 /1814	*55.70*	859/1803	*47.60%*	709/1763	*40.20%*	456/1812	*25.20%*	429/1735	*24.70%*	173/1717	*10.10%*
65-69	1230 / 2107	*58.40%*	793/2094	*37.90%*	760/2039	*37.30%*	547/2099	*26.10%*	460/2005	*22.90%*	207/1994	*10.40%*
70-74	1227 /2086	*58.80%*	605/2073	*29.20%*	692/2013	*34.40%*	525/2069	*25.40%*	398/1994	*20.00%*	219/1957	*11.20%*
75-79	1020 /1670	*61.10%*	387/1654	*23.40%*	524/1619	*32.40%*	378/1665	*22.70%*	256/1605	*16.00%*	184/1578	*11.70%*
80-84	526 / 879	*59.80%*	156/872	*17.90%*	205/853	*24.00%*	182/876	*20.80%*	104/850	*12.20%*	101/849	*11.90%*
85-89	169 /309	*54.70%*	49/307	*16.00%*	61/296	*20.60%*	49/309	*15.90%*	34/296	*11.50%*	30/297	*10.10%*
90-94	36 / 71	*50.70%*	10/71	*14.10%*	10/70	*14.30%*	7/71	*9.90%*	5/70	*7.10%*	4/66	*6.10%*
Total	**8081/15351**	***52.20%***	**7166/15263**	***47.00%***	**5714/14866**	***38.40%***	**3327/15281**	***21.80%***	**3235/14671**	***22.10%***	**1417/14523**	***9.80%***

Table 24. Distribution by Killip Class on Admission in 15191 RO-STEMI Patients

	Killip 1	Killip 2	Killip 3	Killip 4	TOTAL
Patients	10382	2682	1205	922	15191
%	*68.34%*	*17.65%*	*7.93%*	*6.06%*	*100.00%*

Table 25a. Distribution by Killip Class on Admission in 15191 RO-STEMI Patients, by Development Region

	1	2	3	4	5	6	7	8	TOTAL
Validated	1104	1657	452	748	1703	794	1833	6900	15191
Killip 1	824	1113	289	548	881	398	1439	4890	10382
%	*74.63*	*68.19*	*63.93*	*73.26*	*51.73*	*50.12*	*78.50*	*70.86*	*68.34*
Killip 2	158	347	135	145	409	217	276	995	2682
%	*14.31*	*20.94*	*29.86*	*19.38*	*24.10*	*27.32*	*15.05*	*14.42*	*17.65*
Killip 1+2	**982/1104**	**1460/1657**	**424/452**	**693/748**	**1290/1703**	**615/794**	**1715/1833**	**5930/6945**	**13064/15191**
%	*88.94*	*88.11*	*93.80*	*92.64*	*75.74*	*77.45*	*93.56*	*85.38*	*85.99*
Killip 3	43	102	21	27	293	86	58	575	1205
%	*3.89*	*6.15*	*4.64*	*3.60*	*17.20*	*10.83*	*3.16*	*8.33*	*7.93*
Killip 4	79	95	7	28	120	93	60	440	922
%	*7.15*	*5.73*	*1.54*	*3.74*	*7.04*	*11.74*	*3.27*	*6.37*	*6.06*
Killip 3+4	**122/1104**	**197/1657**	**28/452**	**55/748**	**413/1703**	**179/794**	**118/1833**	**1015/6900**	**2127/15191**
%	*11.05*	*11.88*	*6.19*	*7.35*	*24.25*	*22.57*	*6.43*	*14.70*	*13.99*

Table 25b. Distribution by Killip Class on Admission in 16693 RO-STEMI Patients by Development Region (Patients in Table 25a cumulated with patients from The Heart Institute, Cluj-Napoca)

	1	2	3	4	5	6	7	8	TOTAL
Patients	1104	1657	452	748	1703	2296	1833	6945	16693
Killip 1,2	982	1460	424	693	1290	1817	1715	5930	14311
%	*88.94*	*88.11*	*93.80*	*92.64*	*75.74*	*79.13*	*93.56*	*85.38*	*85.50*
Killip 3,4	122	197	28	55	413	479	118	1015	2427
%	*11.05*	*11.88*	*6.19*	*7.35*	*24.25*	*20.86*	*6.43*	*14.70*	*14.49*

Table 26. RO-STEMI Patient Distribution by Type of Treatment in the Interval 1997-2009

Year	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	TOTAL
Total Patients	145	199	374	833	725	771	1029	2263	1506	3380	2385	3017	2887	19510
Conservative	0	0	82	298	269	318	571	1220	770	1881	1328	1636	1319	9692
%	*0.00%*	*0.00%*	*21.92%*	*35.77%*	*37.10%*	*41.24%*	*55.49%*	*53.91%*	*51.12%*	*55.65%*	*55.68%*	*54.22%*	*45.68%*	*49.67%*
Thrombolysis	145	199	292	535	456	440	442	868	525	1131	707	865	629	7234
%	*100.00%*	*100.00%*	*78.08%*	*64.23%*	*64.22%*	*57.06%*	*42.95%*	*38.35%*	*34.86%*	*33.46%*	*29.64%*	*28.67%*	*21.78%*	*35.07%*
Angioplasty	0	0	0	0	0	13	16	175	211	368	336	516	890	2525
%	*0.00%*	*0.00%*	*0.00%*	*0.00%*	*0.00%*	*1.68%*	*1.55%*	*7.73%*	*14.01%*	*10.88%*	*14.08%*	*17.10%*	*30.82%*	*12.94%*
Unknown	0	0	0	0	0	0	0	0	0	0	13	0	46	59
%	*0.00%*	*0.00%*	*0.00%*	*0.00%*	*0.00%*	*0.00%*	*0.00%*	*0.00%*	*0.00%*	*0.00%*	*0.58%*	*0.00%*	*1.69%*	*0.30%*

Table 27. RO-STEMI Patient Distribution by Type of Treatment

	Conservative	Thrombolysis	Angioplasty	Unknown	TOTAL
Patients	9692	7234	2525	59	19510
%	*49.66%*	*37.07%*	*12.93%*	*0.32%*	*100.00%*

Table 28. RO-STEMI Patient Distribution by Economic Area and Type of Therapy

Region	Conservative	Thrombolysis	Angioplasty	Unknown	TOTAL
1	591	404	138	16	1149
%	*51.43%*	*35.16%*	*12.01%*	*1.39%*	*100.00%*
2	450	1205	0	1	1656
%	*27.17%*	*72.76%*	*0.00%*	*0.01%*	*100.00%*
3	126	300	0	26	452
%	*27.87%*	*66.37%*	*0.00%*	*5.75%*	*100.00%*
4	326	421	0	0	747
%	*43.41%*	*56.35%*	*0.00%*	*0.00%*	*100.00%*
5	1315	361	27	0	1703
%	*77.21%*	*21.19%*	*1.58%*	*0.00%*	*100.00%*
6	798	326	1576	1	2701
%	*29.54%*	*12.06%*	*58.34%*	*0.00%*	*100.00%*
7	2992	689	465	15	4161
%	*71.90%*	*16.55%*	*11.17%*	*0.36%*	*100.00%*
8	3094	3528	319	0	6941
%	*44.57%*	*50.82%*	*100.00%*	*0.00%*	*100*
TOTAL	**9692**	**7234**	**2525**	**59**	**19510**
%	*49.67%*	*37.07%*	*12.94%*	*0.30%*	*100.00%*

Table 29. Comparison Between The Demographic Characteristics Of RO-STEMI Patients Treated Conservatively, By Trombolysis, Or By Primary Angioplasty

	Conservative		Thrombolysis		Angioplasty	
	No.	%	No.	%	No.	%
Patients	9689	100.00	7234	100.00	2522	100.00
Age	66.25+/-10	NA	57.93+/-11	NA	58.4+/-11	NA
> 75 years	2476/9245	26.78	727/7092	10.25	130/1020	12.74
Females	3271/9245	35.38	1849/7092	26.07	707/2522	28.03
HTN	4748/8881	53.46	3756/7013	53.55	1306/2325	56.17
Smoking	3420/8819	38.77	3503/7035	49.79	1378/2323	59.31
Dyslipidaemia	3065/8604	35.62	2767/7015	39.44	1153/2277	50.63
Diabetes	2060/8833	23.32	1343/7015	19.14	577/2323	24.83
Previous IM	818/7357	11.11	522/6393	8.16	72/711	10.12
Killip 3 or 4	1413/7678	18.4	639/6903	9.25	66/711	9.28
Onset-admission (Median. min.)	600	NA	155	NA	260	NA
Admission-therapy (Mean. min.)	33+/-41	NA	47+/-40	NA	103+/-69	NA

Table 30. The Ratio Streptokinase/Fibrin-specific Fibrinolytics in 6926 RO-STEMI Patients Treated with Fibrinolytics in the Interval 1997-2009

	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	TOTAL
Patients	145	199	292	535	455	440	442	840	496	1090	687	688	617	6926
SK	145	199	257	443	401	396	330	461	273	628	450	300	266	4549
%	*100.00*	*100.00*	*88.01*	*82.80*	*88.13*	*90.00*	*74.66*	*54.88*	*55.04*	*57.61*	*65.50*	*43.40*	*43.11*	*65.68*
Fibrin-specific	0	0	35	92	54	44	112	379	223	462	237	388	351	2377
%	*0.00*	*0.00*	*11.99*	*17.20*	*11.87*	*10.00*	*25.34*	*45.12*	*44.96*	*42.39*	*34.50*	*56.60*	*56.89*	*34.32*

Table 31. The Main Characteristics of RO-STEMI Patients Treated by Thrombolysis (MI = Myocardial Infarction)

	Streptokinase		Alteplase		Reteplase		Tenecteplase	
	No.	%	No.	%	No.	%	No.	%
Patients	4510	100	961	100	1119	100	400	100
Over 75 years	553	12.26	66	6.87	82	7.33	34	8.5
Females	1194	26.47	240	24.97	279	24.93	104	26
Age (n +/- SD)	60.32±11.91	NA	57.04±11.5	NA	57.52±11.86	NA	58.56±11.73	NA
Anterior STEMI	2161	47.92	502	52.24	577	51.56	210	52.5
Hypertension	2205	48.89	488	50.78	561	50.13	217	54.25
Smoking	2259	50.09	593	61.71	618	55.23	231	57.75
Dyslipidaemia	1644	36.45	398	41.42	499	44.59	177	44.25
Diabetes	845	18.74	165	17.17	226	20.2	93	23.25
Previous MI	297	6.59	116	12.07	81	7.24	33	8.25
Killip 3	230	5.1	47	4.89	56	5	12	3
Killip 4	203	4.5	38	3.95	43	3.84	19	4.75

Table 32. Mean Age and the Proportion of Patients in Killip Classes 3 and 4 on Admission in the RO-STEMI Subgroups Treated with Four Different Streptokinase Regimens or with Fibrin-specific Fibrinolytics

Years 2005 - 2009	1.5 MU/60 min.		1.5 MU/30 min.		SK 1.5 MU/20 min.		SK 0.75 MU/10 min.		Alteplase		Reteplase		Tenecteplase	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Patients	582	100	437	100	312	100	379	100	482	100	883	100	393	100
Age	61+/-12	NA	60+/-12	NA	58+/-13	NA	62+/-13	NA	57+/-12	NA	58+/-12	NA	58,8+/-12	NA
Killip 3	26	4,46	13	2,97	16	5,12	23	6,06	21	4,82	44	4,98	12	3,05
Killip 4	18	3,09	20	4,57	8	2,56	24	6,33	22	4,56	36	4,07	19	4,83

Table 33. Degree of Utilization of Anticoagulants, Antiplatelet Agents, Beta-blockers, ACE-inhibitors, and Statins in RO-STEMI Patients in the Interval 1997-2009

	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	TOTAL
Anticoagulants	129/145	195/199	365/374	790/833	705/725	742/771	988/1029	2006/2122	1270/1331	2861/3109	2010/2117	1935/2047	2142/2232	16138/17034
%	*88.96%*	*97.98%*	*97.59%*	*94.83%*	*97.24%*	*96.23%*	*96.01%*	*94.53%*	*95.41%*	*92.02%*	*94.94%*	*94.52%*	*95.96%*	*94.74%*
Antiplatelets	11/142	22/197	169/363	779/827	633/727	634/762	891/1024	2095/2254	1385/1504	3017/3380	1850/1951	1953/2015	2343/2438	15771/17584
%	*7.74%*	*11.16%*	*46.55%*	*94.19%*	*87.07%*	*83.20%*	*87.01%*	*92.94%*	*92.08%*	*89.26%*	*94.82%*	*96.92%*	*96.10%*	*89.68%*
Beta-blockers	8/142	10/187	143/363	519/827	480/716	526/761	628/1024	1202/1700	687/999	2076/2843	1349/1728	1443/1791	1597/2072	11944/16555
%	*5.63%*	*5.34%*	*39.39%*	*62.75%*	*67.03%*	*69.11%*	*61.32%*	*70.70%*	*68.76%*	*73.02%*	*78.06%*	*80.56%*	*77.07%*	*72.14%*
ACE-I	6/142	10/187	134/363	554/827	542/716	516/761	704/1024	1210/1700	689/999	1974/2842	1369/1728	1424/1791	1565/2072	11903/16654
%	*4.22%*	*5.39%*	*36.91%*	*66.98%*	*75.69%*	*67.80%*	*68.75%*	*71.17%*	*68.96%*	*69.45%*	*79.22%*	*79.50%*	*75.53%*	*71.14%*
Statins	0/145	0/199	107/362	258/823	315/716	437/761	546/1024	1027/1700	594/999	2236/2843	1477/1728	1619/1791	1772/2071	11122/16619
%	*0.00%*	*0.00%*	*29.55%*	*31.34%*	*43.99%*	*57.42%*	*53.32%*	*60.41%*	*59.45%*	*78.64%*	*85.47%*	*90.39%*	*85.56%*	*66.92%*

Table 34. Utilization of Anticoagulants in RO-STEMI Patients in the Interval 1997 - 2009

	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	TOTAL
Validated/total	145/145	199/199	374/374	833/833	725/725	771/771	1029/1029	2122/2263	1331/1506	3109/3380	1727/2385	1784/3017	2006/2883	16155/19510
%	*100.00%*	*100.00%*	*100.00%*	*100.00%*	*100.00%*	*100.00%*	*100.00%*	*93.76%*	*88.37%*	*91.98%*	*72.41%*	*59.13%*	*69.58%*	*82.80%*
No Anticoag.	0	4	9	43	20	29	41	116	61	248	107	112	90	880
%	*0.00%*	*2.00%*	*2.41%*	*5.17%*	*2.76%*	*3.76%*	*4.00%*	*5.46%*	*4.58%*	*7.97%*	*6.20%*	*6.28%*	*4.49%*	*5.44%*
Heparin	129	112	278	549	523	613	712	1250	1015	1423	696	490	419	8209
%	*88.97%*	*56.29%*	*74.34%*	*65.91%*	*72.14%*	*79.50%*	*69.20%*	*58.90%*	*76.25%*	*45.77%*	*40.30%*	*27.47%*	*20.89%*	*50.81%*
Enoxaparin	16	83	38	87	123	123	236	508	215	794	507	750	954	4434
%	*11.03%*	*41.71%*	*10.16%*	*10.41%*	*16.95%*	*15.96%*	*22.90%*	*23.93%*	*16.15%*	*25.53%*	*29.40%*	*42.00%*	*47.56%*	*27.44%*
Hep + Enox	0	0	1	52	0	2	1	57	1	607	311	315	461	1808
%	*0.00%*	*0.00%*	*0.27%*	*6.25%*	*0.00%*	*0.26%*	*0.10%*	*2.68%*	*0.01%*	*19.52%*	*18.00%*	*17.65%*	*22.99%*	*11.19%*
Other	0	0	48	102	59	4	38	191	39	37	106	117	82	823
%	*0.00%*	*0.00%*	*12.83%*	*12.24%*	*8.13%*	*0.51%*	*3.69%*	*9.00%*	*2.93%*	*1.33%*	*6.13%*	*6.55%*	*4.08%*	*5.09%*

Table 35. Utilization of Antiplatelet Agents in RO-STEMI Patients in the Interval 1997 - 2009

	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	TOTAL
Validated/Total	142/145	197/199	363/374	827/833	716/725	762/771	1024/1029	2254/2263	1504/1506	3380/3380	1951/2385	2015/3017	2438/2883	17573/19510
%	*97,93%*	*98,99%*	*97,05%*	*99,27%*	*98,75%*	*98,83%*	*99,51%*	*99,60%*	*99,86%*	*100,00%*	*81,80%*	*66,78%*	*84,56%*	*90,07%*
N antipl.	131	175	194	48	83	120	127	158	119	363	101	57	94	1639
%	*92,25%*	*88,83%*	*53,44%*	*5,80%*	*11,59%*	*15,74%*	*12,40%*	*7,01%*	*7,91%*	*10,74%*	*5,17%*	*2,82%*	*3,85%*	*9,32%*
Aspirin	11	22	168	746	613	542	727	1518	842	1583	610	333	344	8048
%	*7,74%*	*11,16%*	*46,28%*	*90,20%*	*85,61%*	*71,12%*	*70,99%*	*67,34%*	*55,98%*	*46,83%*	*31,26%*	*16,52%*	*14,10%*	*45,76%*
Clopidogrel	0	0	1	10	11	31	12	27	12	57	44	63	68	336
%	*0,00%*	*0,00%*	*0,27%*	*1,20%*	*1,53%*	*4,07%*	*1,17%*	*1,19%*	*0,79%*	*1,68%*	*2,25%*	*3,12%*	*2,78%*	*1,91%*
Asp + Clop	0	0	0	23	8	38	135	526	511	1355	1188	1549	1920	7253
%	*0,00%*	*0,00%*	*0,00%*	*2,78%*	*1,11%*	*4,98%*	*13,18%*	*23,33%*	*33,97%*	*40,08%*	*60,89%*	*76,87%*	*78,75%*	*41,24%*
Other	0	0	0	0	1	23	17	24	20	22	8	8	11	134
%	*0,00%*	*0,00%*	*0,00%*	*0,00%*	*0,14%*	*3,01%*	*1,66%*	*1,06%*	*1,33%*	*0,65%*	*0,41%*	*0,39%*	*0,45%*	*0,76%*
TOTAL antipl.	11	22	169	779	633	634	891	2095	1385	3017	1850	1953	2343	15782
%	*7,74%*	*11,16%*	*46,55%*	*94,19%*	*88,40%*	*83,20%*	*87,01%*	*92,94%*	*92,08%*	*89,26%*	*94,82%*	*96,92%*	*96,10%*	*89,80%*
GPIIbIIIa Inhib.	0/142	0	0	0	11	10	6	42	82	86	45	34	110	426
%	*0,00%*	*0,00%*	*0,00%*	*0,00%*	*1,53%*	*1,31%*	*0,58%*	*1,86%*	*5,45%*	*2,54%*	*2,30%*	*1,68%*	*4,51%*	*2,42%*
Unknown	3/145	2/199	11/374	6/833	9/725	9/771	5/1029	9/2263	2/1506	0/3380	434/2385	1002/3017	445/2883	1937/19510
%	*2,06%*	*1,01%*	*2,94%*	*0,72%*	*1,24%*	*1,16%*	*0,48%*	*0,39%*	*0,13%*	*0,00%*	*18,19%*	*33,21%*	*15,43%*	*9,90%*
TOTAL patients	145	199	374	833	725	771	1029	2263	1506	3380	2385	3017	2883	19510

Table 36. Administration Rate of Anticoagulants, Antiplatelet Agents, ACE-I agents, Beta-blockers and Statins in Patients Treated Conservatively, by Thrombolysis or by Primary Angioplasty

	Conservative		Thrombolysis		Angioplasty	
	No.	%	No.	%	No.	%
Anticoagulants	8369/9013	92.85	6637/6879	96.48	689/708	97.13
Heparin	*3064/7446*	*41.14*	*3799/6879*	*55.22*	*269/708*	*37.99*
Eoxaparin	*2802/7446*	*37.63*	*1427/6879*	*20.74*	*180/708*	*25.42*
Hep. + Enox.	*729/7446*	*9.79*	*859/6879*	*12.48*	*204/708*	*28.81*
Other	*232/7446*	*3.11*	*794/6879*	*11.54*	*36/708*	*5.08*
Antiplatelet agents	8121/8968	90.55	5886/6775	86.87	2142/2165	98.93
Aspirin	*3858/7401*	*52.12*	*3169/6775*	*46.77*	*23/663*	*3.46*
Clopidogrel	*151/7401*	*2.04*	*157/6775*	*2.31*	*13/663*	*1.96*
Asp. + Clop.	*2476/7401*	*33.45*	*2489/6775*	*36.73*	*487/663*	*73.45*
Other	*69/7401*	*0.93*	*71/6775*	*1.04*	*133/663*	*20.06*
Beta-blockers	5128/7561	67.82	4888/6830	71.56	2092/2212	94.57
ACE-I	5175/7561	68.44	4843/6829	70.91	1905/2212	86.12
Statins	5042/7559	66.7	4645/6807	68.23	1589/2212	71.83
CVA	84/7542	1.11	74/6848	1.08	8/815	0.98
Major Haemor.	49/7465	0.64	167/6795	0.68	10/712	1.4
Post-MI angina	660/7123	9.26	889/6529	13.61	21/664	3.16
Reinfarction	10/3205	0.31	137/6718	2.03	15/617	2.43
Coronary Angiography	1175/7639	15.38	1020/6852	14.88	NA	NA
Angioplasty	660/7639	8.63	504/6834	7.37	NA	NA
Stent Deployment	628/7639	8.22	485/6834	7.09	NA	NA
Mortality	1449/9459	15.31	659/7193	9.16	166/2522	6.58

Table 37. Administration Rate for Anticoagulants, Antiplatelet Agents, Beta-blockers, ACE-I agents, and Statins in Patients Treated with Thrombolytics

	Streptokinase		Alteplase		Reteplase		Tenecteplase	
	No.	%	No.	%	No.	%	No.	%
Anticoagulants	4485	99.45	957	99.58	1099	98.21	400	100.00
None	*160*	*3.55*	*27*	*2.81*	*35*	*3.13*	*20*	*5.00*
Heparin	*2722*	*60.35*	*462*	*48.07*	*545*	*48.70*	*87*	*21.75*
Enoxaparin	*853*	*18.91*	*233*	*24.25*	*211*	*18.86*	*155*	*38.75*
Heparin and Enoxaparin	*412*	*9.14*	*155*	*16.13*	*193*	*17.25*	*115*	*28.75*
Other	*338*	*7.49*	*80*	*8.32*	*115*	*10.28*	*23*	*5.75*
Antiplatelet agents	4434	98.31	929	96.67	1092	97.59	382	95.50
None	*747*	*16.56*	*84*	*8.74*	*46*	*4.11*	*18*	*4.50*
Aspirin	*2299*	*50.98*	*418*	*43.50*	*369*	*32.98*	*83*	*20.75*
Clopidogrel	*90*	*2.00*	*27*	*2.81*	*32*	*2.86*	*12*	*3.00*
Aspirin and Clopidogrel	*1239*	*27.47*	*379*	*39.44*	*634*	*56.66*	*258*	*64.50*
IIbIIIa Inhibitors	*46*	*1.02*	*18*	*1.87*	*5*	*0.45*	*8*	*2.00*
Other	*13*	*0.29*	*3*	*0.31*	*6*	*0.54*	*3*	*0.75*
Beta-blockers	2957	65.57	716	74.51	933	83.38	328	82.00
ACE-I	2980	66.08	699	72.74	894	79.89	320	80.00
Statins	2683	59.49	715	74.40	945	84.45	353	88.25

Table 38. Annual Rate of Coronary Angiography, Angioplasty, and Stent Deployment in RO-STEMI Patients Treated with Thrombolytics or Conservatively

Procedure	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	TOTAL
Coronary Angiography	0/145	0/199	21/374	28/833	34/725	52/758	97/1013	253/2088	135/1295	469/3012	276/2030	319/2467	511/1875	2195/16814
%	*0.00*	*0.00*	*5.61*	*3.36*	*4.69*	*6.86*	*9.58*	*12.12*	*10.42*	*15.57*	*13.60*	*12.93*	*27.25*	*13.05*
Angioplasty	0/145	0/199	12/374	17/831	13/725	33/757	41/1012	108/2074	75/1291	256/3000	104/2030	158/2449	347/1875	1164/16762
%	*0.00*	*0.00*	*3.21*	*2.05*	*1.79*	*4.36*	*4.05*	*5.21*	*5.81*	*8.53*	*4.20*	*6.45*	*18.51*	*6.94*
Stent	0/145	0/199	12/374	17/831	13/725	29/757	41/1012	106/2074	74/1291	247/3000	100/2018	151/2445	325/1798	1022/16669
%	*0.00*	*0.00*	*3.21*	*2.05*	*1.79*	*3.83*	*4.05*	*5.11*	*5.73*	*8.23*	*4.96*	*6.18*	*18.08*	*6.13*

Table 39. Global Rate of Coronary Angiography, Angioplasty, and Stent Deployment in Patients Treated who Initially Received Conservative or Thrombolytic Therapy

	Conservative		Thrombolysis	
	No.	%	No.	%
Coronary Angiography	1175/7639	15.38	1020/6852	14.88
Angioplasty	660/7639	8.63	504/6834	7.37
Stent	628/7639	8.22	485/6834	7.09

Table 40. Global Rate Of Post-MI Complications in RO-STEMI Patients (MI = myocardial infarction)

Post-MI Complications	No. / Validated	%
Post-MI Angina	1506/14914	*10.09%*
Reinfarction	163/14808	*1.10%*
Cardiogenic Shock	249/15017	*1.65%*
Heart failure	3219/14958	*21.50%*
Major Haemorrhage	218/14947	*1.45%*
Stroke (total)	163/15053	*1.08%*
- Haemorrhagic	64/15053	*0.42%*
- Ischaemic	39/15053	*0.26%*
- Ischaemic With Haemorrhagic Transformation	5/15053	*0.003%*
Unknown	55/15053	*0.36%*

Table 41. Incidence of Stroke, of Major Haemorrhage, of Post-MI Angina, and of Reinfarction in RO-STEMI Patients Treated Conservatively, with Thrombolytics, or with Primary Angioplasty

Treatment	Conservative		Thrombolysis		Angioplasty	
	No.	%	No.	%	No.	%
Stroke	84/7542	1.11	74/6848	1.08	8/815	0.98
Major Haemorrhage	49/7465	0.65	167/6795	2.45	10/712	1.4
Post-MI angina	660/7123	9.26	889/6529	13.61	21/664	3.16
Reinfarction	oct.05	0.31	137/6718	2.03	15/617	2.43

Table 42. Incidence of Stroke, Major Haemorrhage, Postinfarction Angina, Cardiogenic Shock, and Reinfarction in RO-STEMI Patients Treated with Streptokinase or with Fibrin-specific Thrombolytics

Thrombolytic	Streptokinase		Alteplase		Reteplase		Tenecteplase	
	No.	%	No.	%	No.	%	No.	%
Patients	4510	64.52	961	13.75	1119	16.01	400	5.72
Stroke	31	0.69	10	1.04	11	0.98	8	2
Haemorrhagic	16	0.35	4	0.42	6	0.54	6	1.5
Ischaemic	8	0.18	2	0.21	2	0.18	0	0
Ischaemic-Haemorrhagic	1	0.02	0	0	1	0.09	0	0
Unknown	6	0.13	4	0.42	2	0.18	2	0.5
Major Haemorrhage	118	2.62	21	2.19	13	1.16	15	3.75
Postinfarction angina	586	12.99	145	15.09	128	11.44	31	7.75
Cardiogenic Shock	45	1	14	1.46	27	2.41	4	1
Reinfarction	86	1.91	23	2.39	16	1.43	13	3.25

Table 43. Annual In-Hospital Mortality in RO-STEMI Patients in the Interval 1997–2009

Year	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	TOTAL
Patients	145	199	374	833	725	771	1029	2263	1506	3380	2385	3017	2883	19510
Fatalities	14	33	64	86	85	102	160	299	204	459	218	345	242	2311
%	*9.65*	*16.58*	*17.11*	*10.32*	*11.72*	*13.22*	*15.54*	*13.21*	*13.54*	*13.57*	*9.14*	*11.43*	*8.39*	*11.84*

Table 44. Global In-Hospital Mortality in RO-STEMI Patients in the Interval 1997–2009 by Development Region

Region	1	2	3	4	5	6	7	8	TOTAL
Patients	1149	1656	452	747	1703	2701	4157	6945	19510
Fatalities	122	175	15	57	232	276	585	849	2311
%	*10.61*	*10.56*	*3.31*	*7.63*	*13.62*	*9.25*	*12.12*	*12.22*	*11.84*

Table 45. Mean Age, Killip III/IV Class, and Global In-Hospital Mortality in RO-STEMI Patients in the Interval 1997–2009 by Development Region

Region	1	2	3	4	5	6	7	8
Age (n +/- SD)	63.34+/ -13.3	59.61+/ -12.5	61.68+/ -12.6	61.36+/ -12.3	62.91+/ -11.8	63.48+/ -12.4	62.92+/ -12.7	62.63+/ -13.1
Killip 3.4 (%)	11.05	11.88	6.19	7.35	24.25	20.86	6.43	14.7
Mortality (%)	10.61	10.56	3.31	7.63	13.62	9.25	12.12	12.22

Table 46. Mean Age, Killip III/IV Class on Admission, and In-Hospital Mortality in RO-STEMI Patients in the Interval 1997-2009 by Development Regions, Grouped as Follows: Regions with A Per Capita GNP < 2800 Euro (Regions 1,2,3,4); Regions with A Per Capita GNP between 2800 and 5600 Euro (Regions 5,6,7); Regions with A Per Capita GNP > 5600 Euro (Region 8)

Region	R 1,2,3,4	R 5,6,7	R 8
Age (n +/- SD)	61.49+/-12	63.10+/-12	62.63+/-13
Killip 3.4 (%)	10.14	17.31	14.70
Mortality (%)	*9.21*	*12.76*	*12.22*

Table 47. In-Hospital Mortality in RO-STEMI Patients Treated Conservatively, with Thrombolytics, or with Primary Angioplasty (* = for 2008. We did not take into account the 271 patients from Sibiu, in whom only global mortality, but not subgroup mortality was known)

	Conservative		Thrombolysis		Angioplasty	
Year	No.	%	No.	%	No.	%
1997	NA	NA	14/145	9.65	NA	NA
1998	NA	NA	33/199	16.58	NA	NA
1999	24/82	29.26	40/292	13.69%	NA	NA
2000	41/298	13.75	45/535	8.41	NA	NA
2001	41/269	15.24	44/456	9.64	NA	NA
2002	52/318	16.35	48/440	10.9	2/13	15.38
2003	95/571	16.63	62/442	14.02	3/16	18.75
2004	214/1220	17.54	69/868	7.94	16/175	9.14
2005	137/770	17.79	52/525	9.9	15/211	7.1
2006	323/1881	17.17	111/1131	9.81	25/368	6.79
2007	138/1328	10.39	56/707	7.92	24/336	7.14
2008*	229/1406	16.28	52/824	6.31	33/516	6.39
2009	155/1319	11.75	33/629	5.24	49/890	5.52
TOTAL	**1449/9462**	**15.31**	**659/7193**	**9.16**	**167/2522**	**6.62**

Table 48. In-hospital Mortality in RO-STEMI Patients in the Interval 2005-2009 by Type of Reperfusion Therapy *(ND=No Data; SK=Streptokinase; tPA=Alteplase; rPA= Reteplase; TNK=Tenecteplase; PCI=Primary Angioplasty)*

Years	SK1.5 MU/60		SK1.5 MU/30		SK1.5 MU/20		SK0.75 MU/10		tPA		rPA		TNK		PCI	
2005 - 2009	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Patients	582	100	437	100	312	100	379	100	482	100	883	100	393	100	2321	100
Mortality	54	9.27	53	12.12	19	6.02	33	8.70	31	6.43	55	6.2	32	8.14	146	6.29
< 75 year	41/500	8.2	38/388	9.79	12/282	4.25	25/311	8.03	25/433	5.77	47/814	5.8	28/359	7.79	ND	ND
> 75 year	13/82	15.85	15/49	30.61	7/30	23.33	8/68	11.76	6/49	12.2	8/69	12	4/34	11.8	ND	ND

Table 49. Comparisons between the Main Demodraphic Characteristics, the Incidence of Coronary Risk Factors, Therapy, and In-Hospital Mortality in RO-STEMI Patients, in three Different Time Intervals

	RO - STEMI 1 (1997-2001)		RO-STEMI 2 (2002-2005)		RO-STEMI 3 (2006-2009)	
	No.	%	No.	%	No.	%
Patients	2276	100	5569	100	11665	100
Age +/- SD	62±12	/	63±13	/	63±13	/
Males	1604	70.47	3782	67.91	7990	68.49
Onset-to-admission (Median. min.)	180	/	210	/	274	/
Hypertension	919	40.37	2766/5251	52.87	5056/9275	54.52
Smoking	954	41.91	2583/5252	49.19	4149/9186	45.17
Dyslipidaemia	613	26.93	1958/5233	37.42	3654/8811	41.47
Diabetes	392	17.22	1075/5251	20.48	2115/9208	22.97
Previous MI	210	9.22	399/4315	9.25	808/8069	10.01
Conservative Treatment	741	32.55	2879	51.69	6164	52.84
Thrombolysis	1627	71.48	2275	40.85	3332	28.56
Primary PCI	0	0	415	7.45	2110	18.08
Total reperfusion	*1627*	*71.48*	*2690*	*48.3*	*5442*	*46.65*
Anticoagulants	2184/2276	95.95	5006/5253	95.29	8948/9505	94.13
Heparin	*1591/2276*	*69.9*	*3590/5253*	*68.34*	*3028/8626*	*35.1*
Enoxaparin	*347/2276*	*15.24*	*1082/5253*	*20.59*	*3005/8626*	*34.83*
Heparin + Enoxoxaparin	*53/2276*	*2.32*	*61/5253*	*1.16*	*1694/8626*	*19.63*
Antiplatelet agents	1614/2245	71.89	4905/5544	88.47	9163/9784	93.65
Aspirin	*1560/2245*	*69.48*	*3629/5544*	*65.45*	*2870/9784*	*29.33*
Clopidogrel	*22/2245*	*0.97*	*82/5544*	*1.47*	*232/9784*	*2.37*
Aspirin + Clopidogrel	*31/2245*	*1.38*	*1210/5544*	*21.82*	*6012/9784*	*61.44*
ACE-I	1246/2235	55.74	3119/4484	69.55	6332/8433	75.08
Beta-blockers	1160/2235	51.9	3043/4484	67.86	6465/8434	76.65
Statins	680/2245	30.28	2604/7088	36.73	7104/8433	84.24
Coronary Angiography*	83/2276	3.64	537/5154	10.41	1575/9384	16.78
Angioplasty*	42/2276	1.84	257/5134	5.00	865/9354	9.24
Stent*	42/2276	1.84	250/5134	4.86	823/9261	8.86
Mortality	282/2276	12.39	765/5569	13.73	1264/11665	10.83

Table 50. Comparative Data between RO-STEMI and other three International Registries Published in the Interval 2000-2009

	RO-STEMI-1 (2000-2001)*	EHS-ACS-1 (2000-2001)	RO-STEMI-2 (2004)	EHS-ACS-2 (2004)	RO-STEMI-3 (2009)	SNAPSHOT (2009)
Patients	1558	4431	2263	3004	2883	1871
Age +/- SD (Median)	62+/-12	63.4+/-13	62.95+/-10.5	62.5+/-13	63.33+/12	63+/-13
Females	29.39%	28.40%	31.72%	25.90%	30.00%	27.00%
Hypertension	49.29%	51.60%	51.83%	50.00%	55.83%	60.00%
Smoking	50.44%	63.10%	49.93%	45.60%	46.31%	39.00%
Dyslipidaemia	34.53%	46.80%	37.60%	43.20%	45.90%	40.00%
Diabetes	21.18%	21.10%	21.65%	21.40%	23.55%	21.00%
Previous MI	10.96%	22.30%	10.69%	15.70%	10.86%	16.00%
Killip III/IV	11.04%	5.80%	17.45%	ND	13.80%	20.00%
Pain-to-admission (Median. min.)	180	210	220	170	255	ND
Conservative Treatment	36.39%	44.20%	53.91%	36.00%	46.54%	30.00%
Thrombolysis	63.60%	35.10%	38.35%	26.23%	22.19%	20.00%
Primary PCI	0.00%	20.71	7.73%	37.76%	31.40%	50.00%
Total reperfusion	63.60%	55.80%	46.09%	63.99%	53.59%	70.00%
Anticoagulants	95.95	86.80%	94.53%	77.20%	95.96%	ND
Antiplatelet agents	91.51%	93.00%	92.99%	96.80%	96.01%	98.00%
Aspirin	*86.58%*	*93.00%*	*71.84%*	*96.80%*	*21.48%*	*98.00%*
Asp. + Clopid.	*1.98%*	*23.30%*	*23.29%*	*69.80%*	*65.69%*	*94.00%*
ACE-I	71.03%	62.10%	71.86%	75.40%	76.36%	83.00%
Beta-blockers	64.74%	77.80%	71.80%	83.00%	78.44%	85.00%
Statins	37.23%	49.20%	60.51%	80.70%	81.59%	92.50%
Coronary Angiography**	3.97%	58.10%	14.76%	70.20%	34.23%	51.00%
Angioplasty* *	1.92%	42.80%	6.30%	57.80%	23.18%	ND
In-hospital Mortality	10.97%	7.00%	13.21%	6.40%	8.39%	8.50%
No reperfusion	*15.34%*	*ND*	*16.91%*	*ND*	*11.72%*	*12.20%*
Thrombolysis	*8.98%*	*ND*	*7.94%*	*ND*	*5.24%*	*9.10%*
Primary PCI	*NA*	*ND*	*9.14%*	*ND*	*5.52%*	*6.10%*

(Patients Treated Mainly with Thrombolytics; ** Procedures in Patients not Undergoing Primary Angioplasty)*

Table 51. Percent Distribution of 12507 RO-STEMI Patients in Three Different Enrollment Periods by Symptom Onset-To-Admission Time

	RO-STEMI-1 (1997–2001)	RO-STEMI-2 (2002-2005)	RO-STEMI-3 (2006-2009)	TOTAL
Patients	1931	3865	6711	12507
Pain-to-admission (Median. min)	180	210	262	240
0 - 179 min	925	1556	2125	4606
%	*47.9*	*40.25*	*31.66*	*36.82*
180 - 359 min.	555	1056	1774	3385
%	*28.74*	*27.32*	*26.43*	*27.06*
360 - 719 min.	230	498	1017	1745
%	*11.91*	*12.88*	*15.15*	*13.95*
720 - 1439 min.	117	303	695	1115
%	*6.05*	*7.83*	*10.35*	*8.91*
>24 hours	104	450	1100	1654
%	*5.38*	*11.64*	*16.39*	*13.22*

Table 52. Comparative Data between RO-STEMI 2009 and SNAPSHOT Patients, Using the Division into three Geographical Areas (North, West, Central and Eastern Europe, Mediterranean Countries)

	RO - STEMI 3. 2009	SNAPSHOT 2009				
	/	North	West	Central/East	Mediterranean	Global
Patients	2883	67	278	918	608	1871
Age+/- SD (Median)	63.33+/12	64+/-12	64+/-13	63+/-12	62+/-14	63+/-13
Females	30.00%	28%	27%	33%	23%	27.00%
Hypertension	55.83%	34%	58%	66%	54%	60.00%
Smoking	46.31%	40%	35%	37%	44%	39.00%
Dyslipidaemia	45.90%	32%	40%	38%	43%	40.00%
Diabetes	23.55%	4.50%	18%	21%	25%	21.00%
Previous MI	10.86%	16%	12%	18%	15%	16.00%
Killip III/IV	13.80%	15%	17%	24%	17%	20.00%
Conservative Treatment	46.54	19%	22%	37%	24%	30.00%
Thrombolysis	22.19%	30%	8.00%	21%	22.50%	20.00%
Onset-to-treatment (Median. min.)	*200*	*145*	*117*	*165*	*170*	*164*
Primary PCI	31.40%	51%	71%	41.50%	55.50%	50.00%
Onset-to-treatment (Median. min.)	*312*	*230*	*305*	*300*	*240*	*270*
Total reperfusion	54.59%	56.50%	78%	62.50%	78.00%	70.00%
Aspirin	21.48%	0.00%	1.00%	2.50%	1.00%	98.00%
Asp. + Clopid.	65.69%	100%	99%	90.50%	97%	94.00%
ACE-I	76.36%	70.00%	81.00%	84.00%	84.00%	83.00%
Beta-blockers	78.44%	95.50%	87.00%	84.00%	84.00%	85.00%
Statins	81.59%	98.50%	90.00%	92.00%	94.00%	92.50%
Coronary Angiography*	34.23%	85.00%	100.00%	35.00%	61.00%	51.00%
In-hospital Mortality	8.39%	4.30%	6.10%	10.00%	7.90%	8.50%

(= Coronary Angiography in Patients Treated with Thrombolytics or Conservatively)*

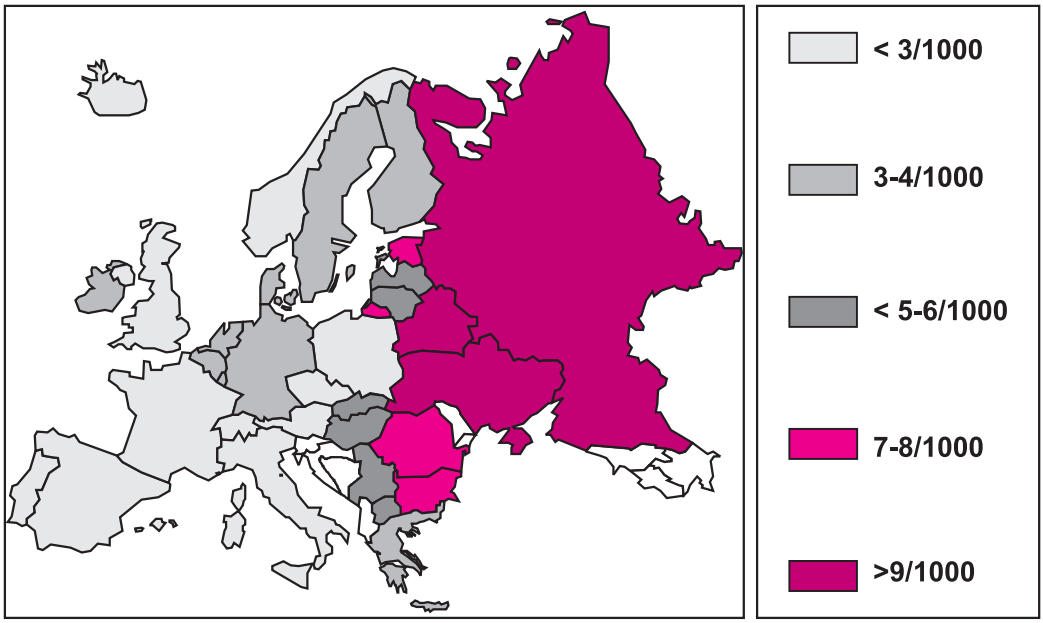

Figure 1. Cardiovascular Mortality in Europe
(European Society of Cardiology, Cardiovascular diseases in Europe, 2006)

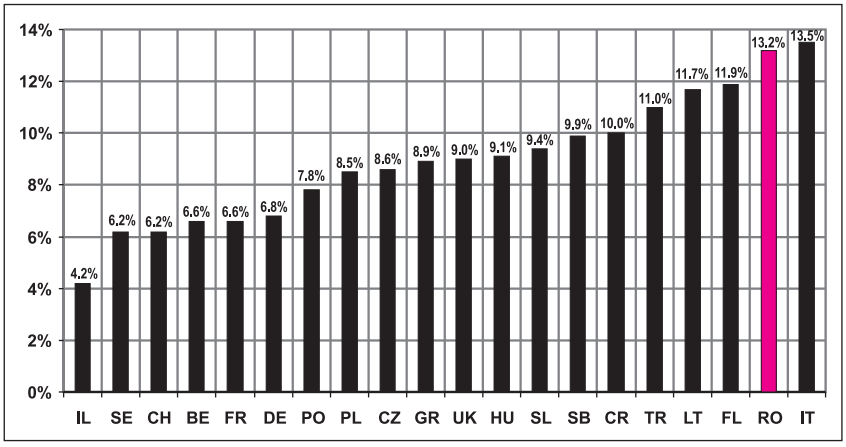

Figure 2. In-hospital acute myocardial infarction mortality in European countries (9)

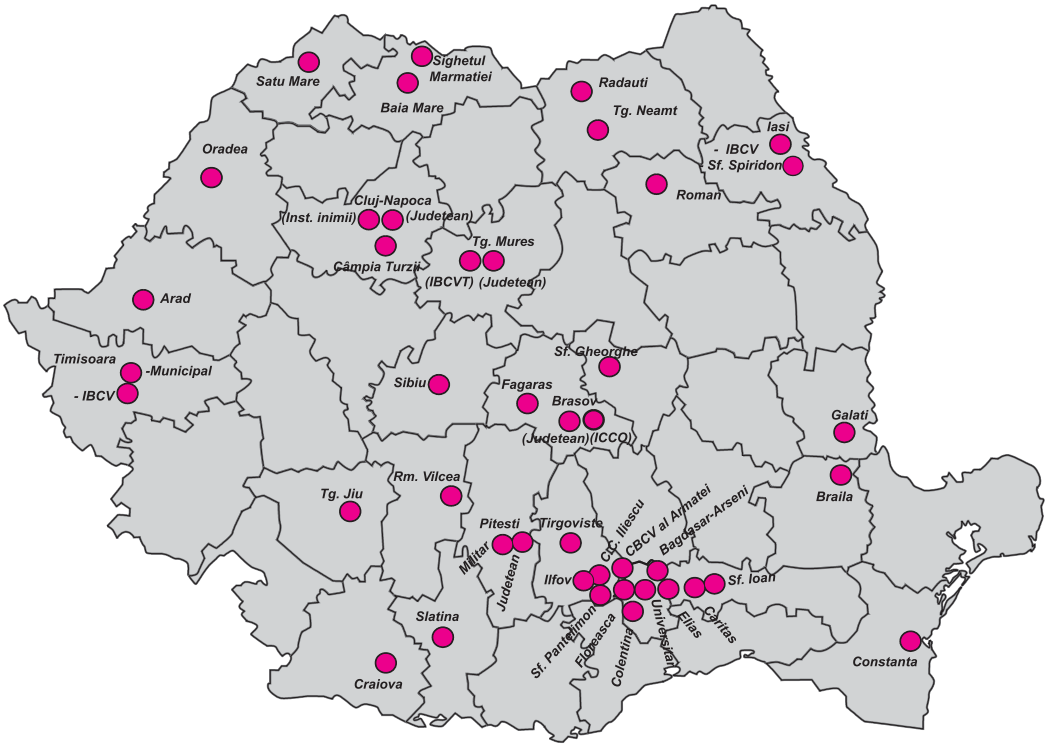

Figure 3. RO-STEMI Centers

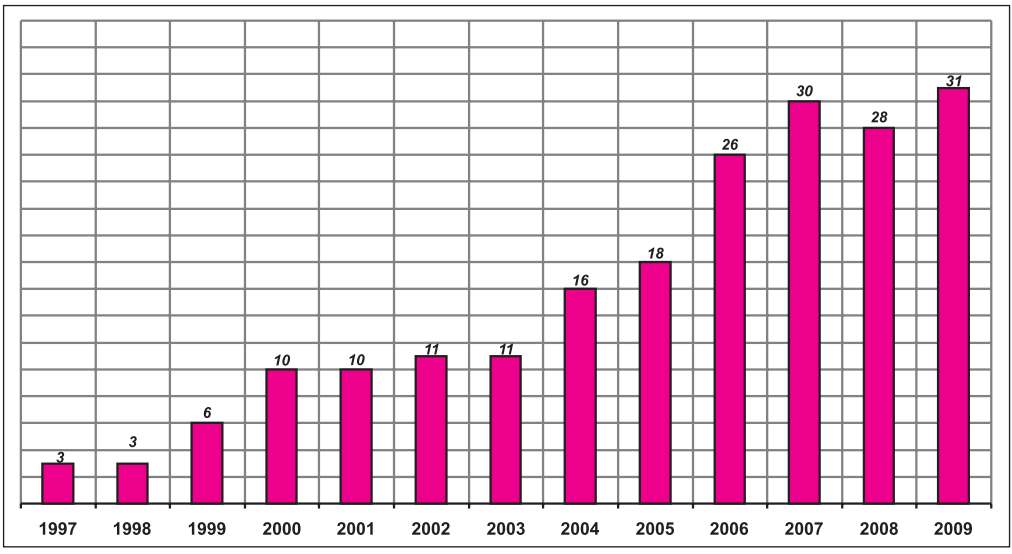

Figure 4. Number of active RO-STEMI centers for each year between 1997-2009

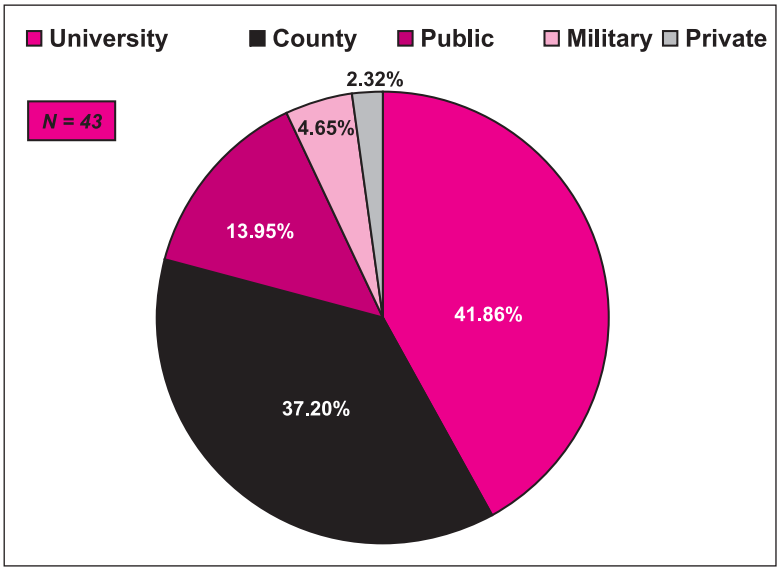

Figure 5. Percent representation of the five types of RO-STEMI centers (traditional university, county, municipal/city, military or private centers)

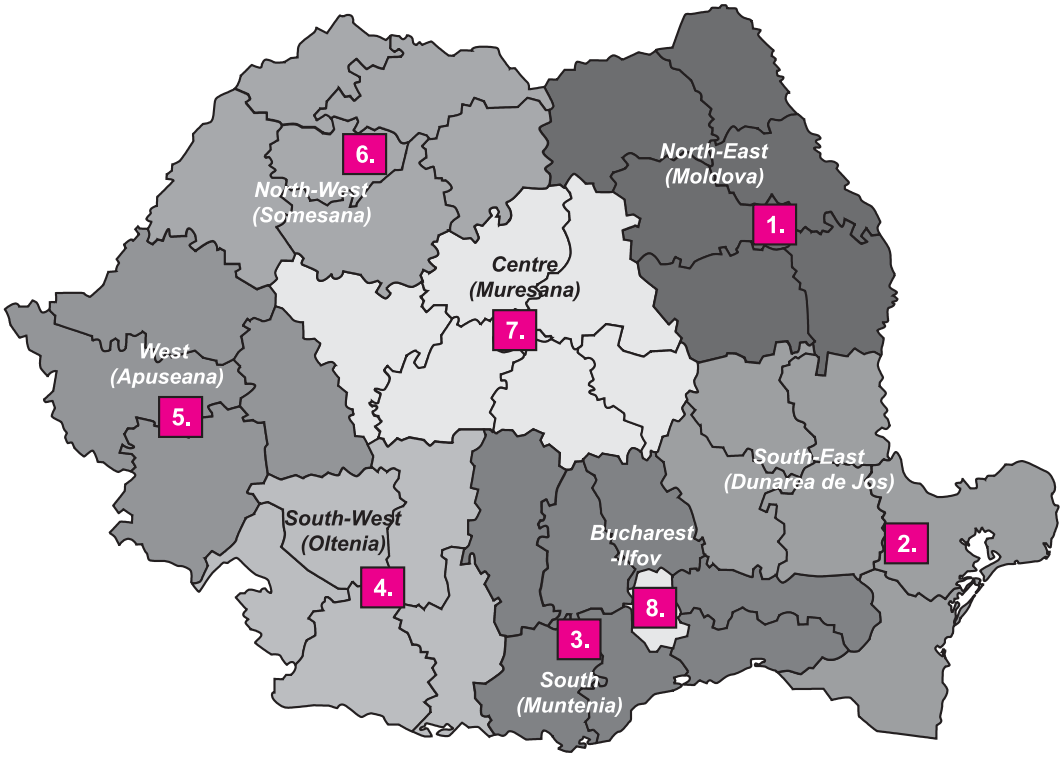

Figure 6. The 8 Development Regions in Romania (14)

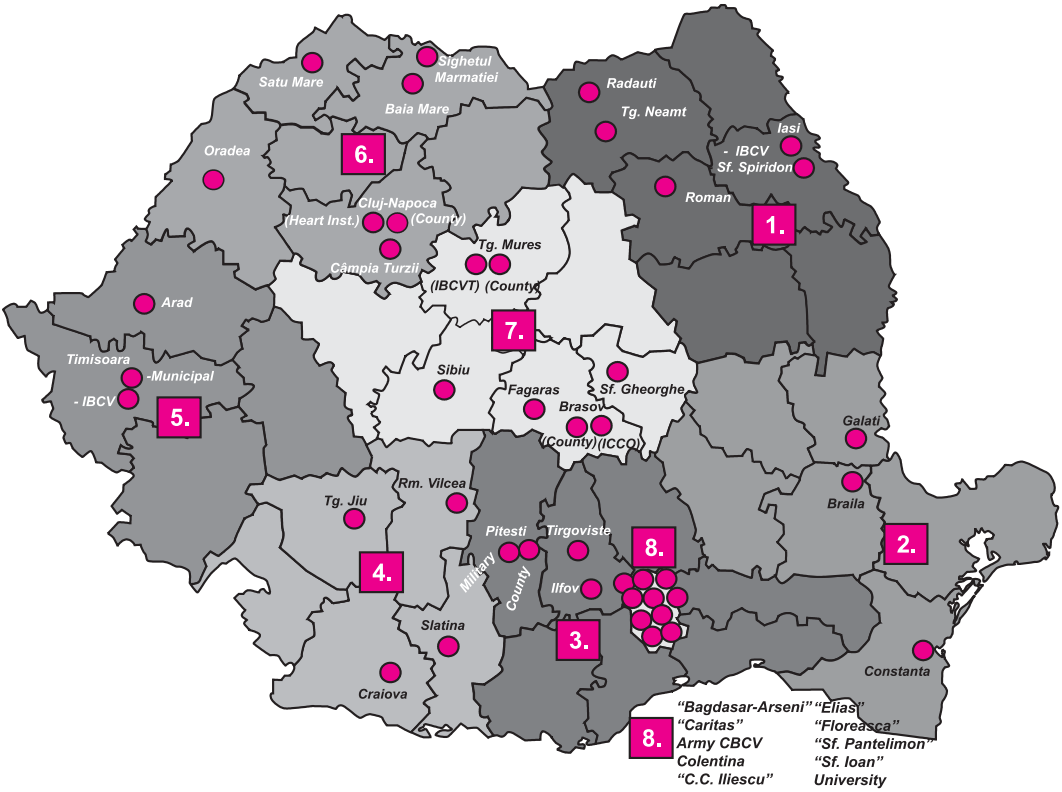

Figure 7. Distribution of RO-STEMI centers in the 8 Development Regions of Romania

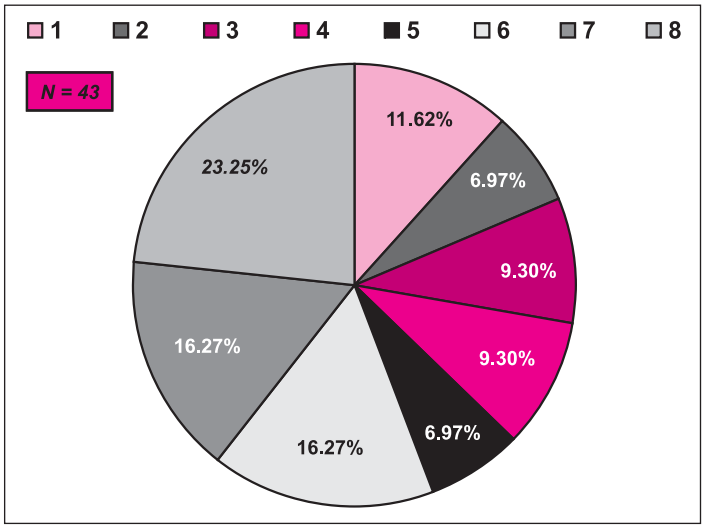

Figure 8. Percent distribution of RO-STEMI centers according to the 8 Development Regions in Romania

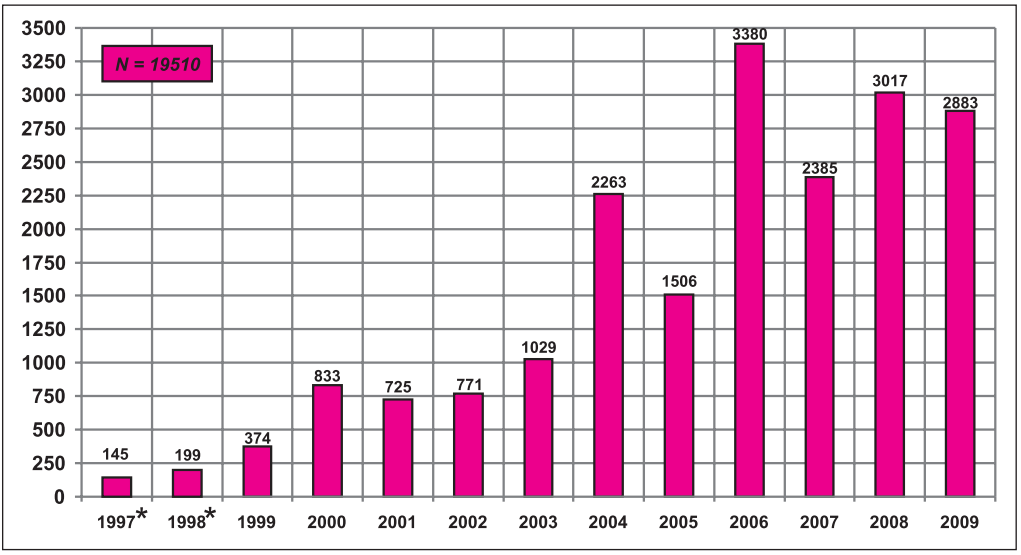

Figure 9. Yearly enrolment rate of RO-STEMI patients (*only patients treated with thrombolytics)

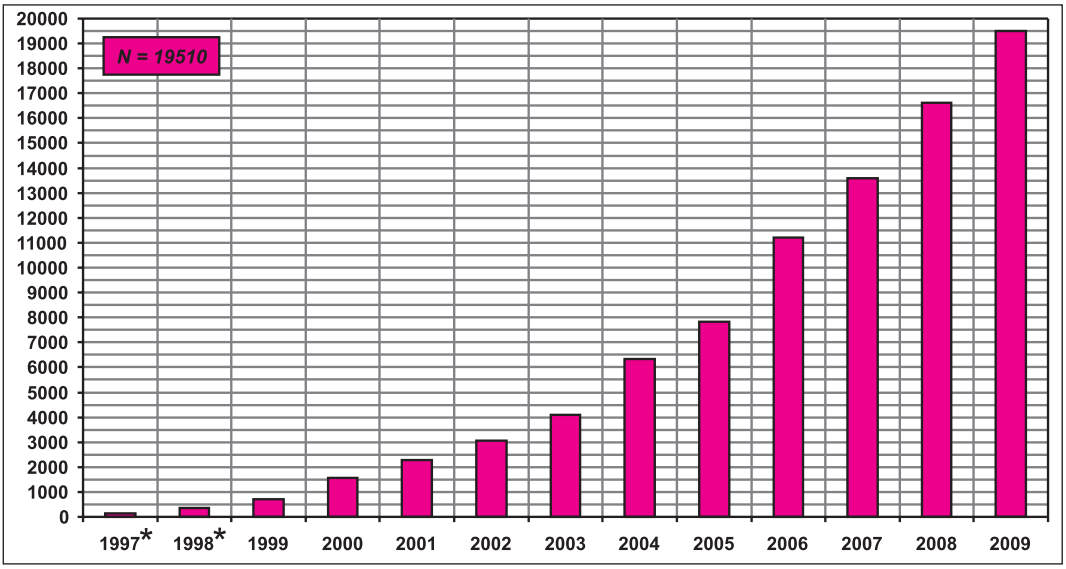

Figure 10. Cumulative enrolment rate of RO-STEMI patients (*only patients treated with thrombolytics)

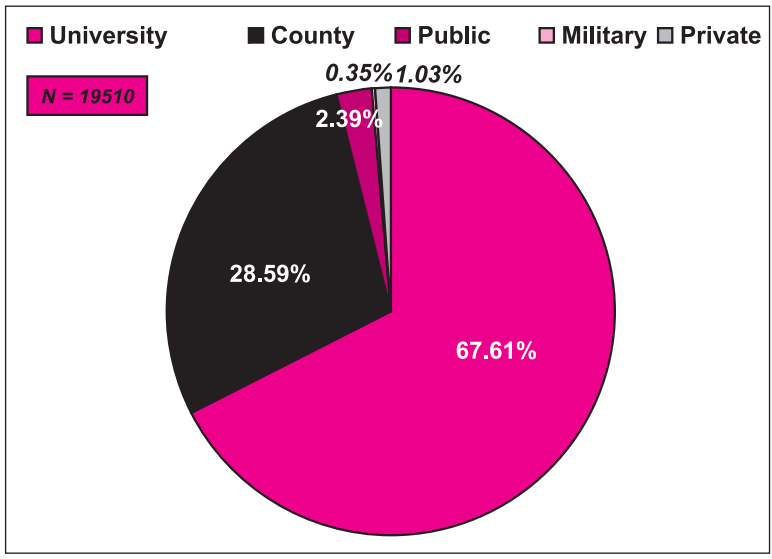

Figure 11. Percent distribution of RO-STEMI patients by type of hospital

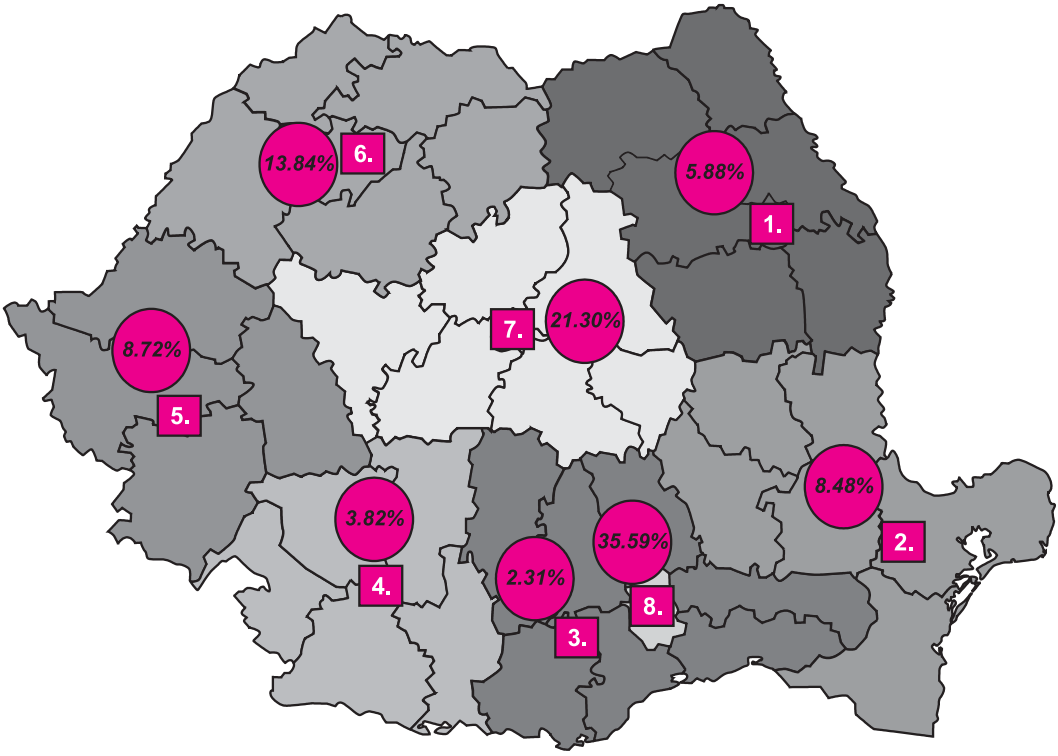

Figure 12. RO-STEMI patient distribution by the 8 Development Regions in Romania

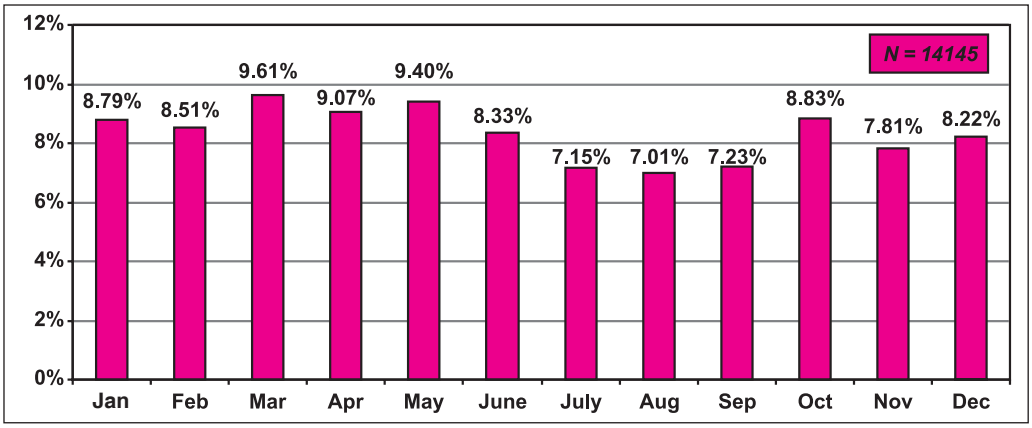

Figure 13. Percent distribution of 14145 RO-STEMI patients by month of admission

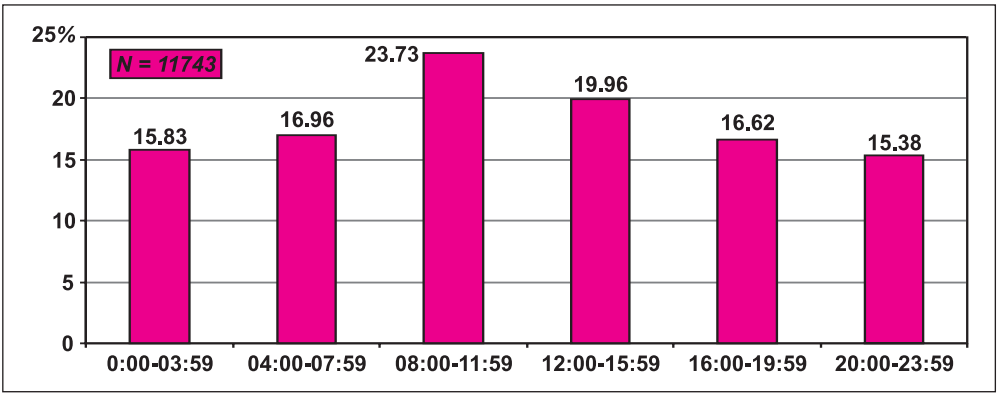

Figure 14. Percent distribution of 11743 RO-STEMI patients by the time of infarction onset

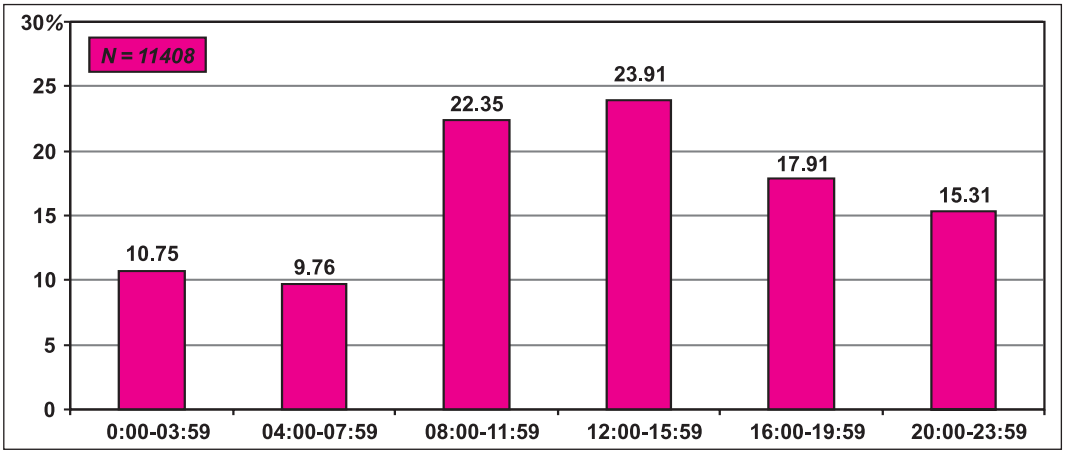

Figure 15. Percent distribution of 11408 RO-STEMI patients by the time of admission

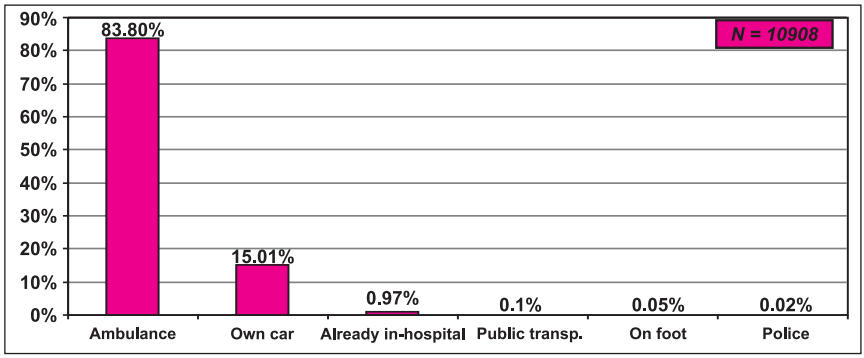

Figure 16. Percent distribution of 10908 RO-STEMI patients by the type of transport to the hospital

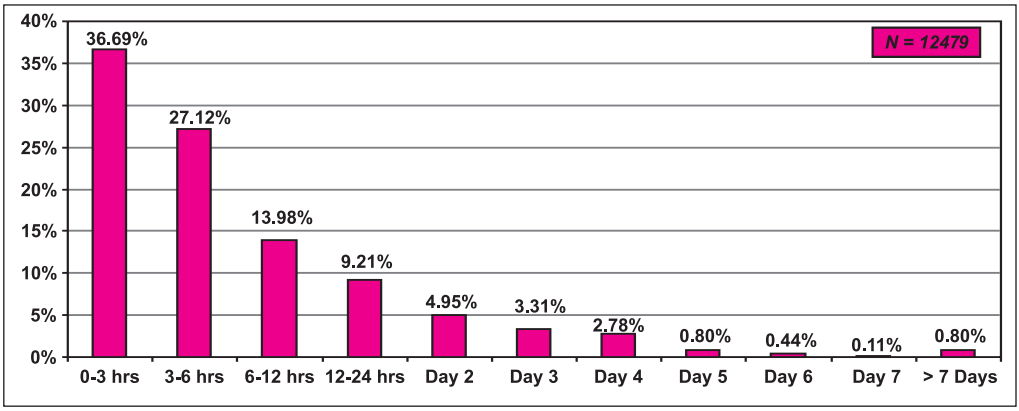

Figure 17. Percent distribution of 12479 RO-STEMI patients by chest pain-to-admission time

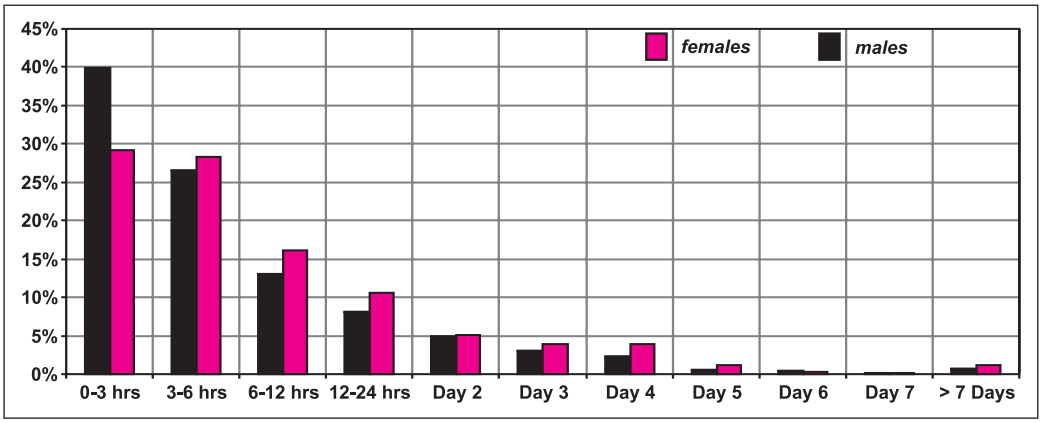

Figure 18. Percent distribution of 12479 RO-STEMI patients by gender and chest pain-to-admission time

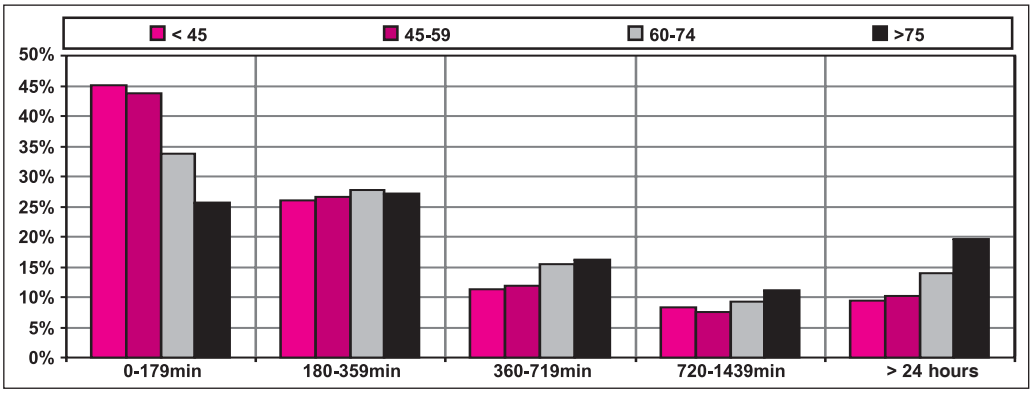

Figure 19. Percent distribution of 12479 RO-STEMI patients by age group and chest pain-to-admission time

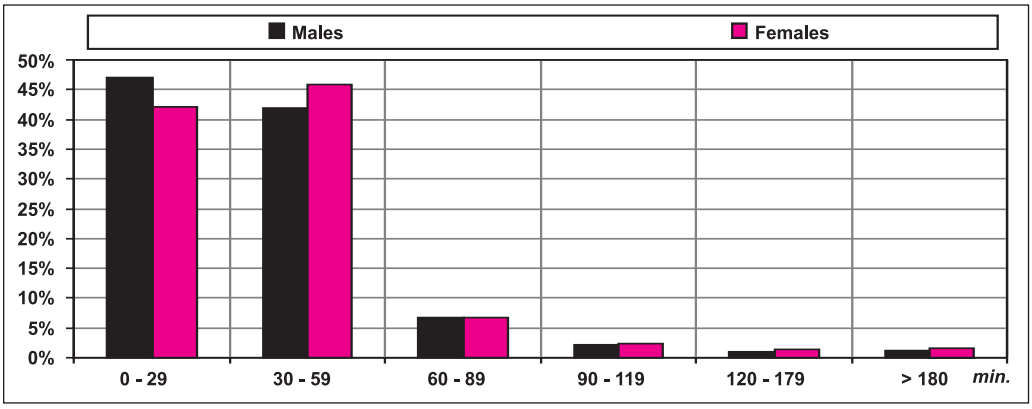

Figure 20. Percent distribution of 12063 RO-STEMI patients by gender and admission-to-treatment onset time

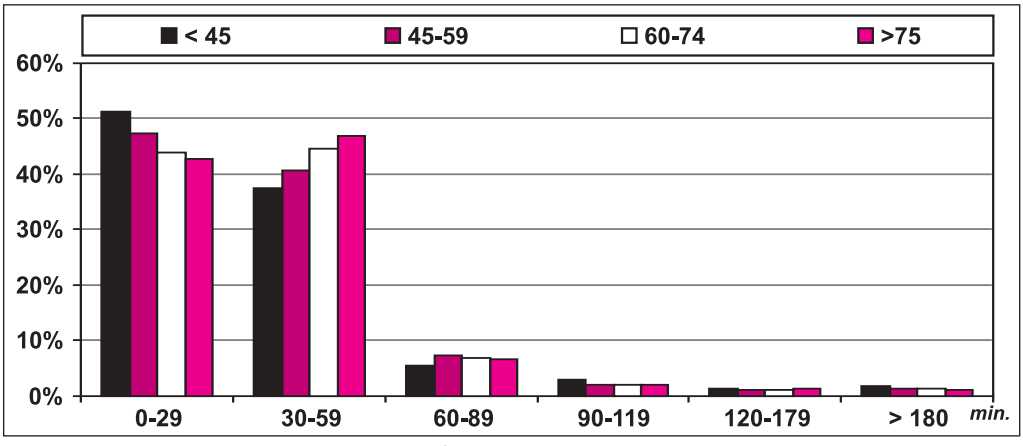

Figure 21. Percent distribution of 12063 RO-STEMI patients by age group and admission-to-treatment onset time

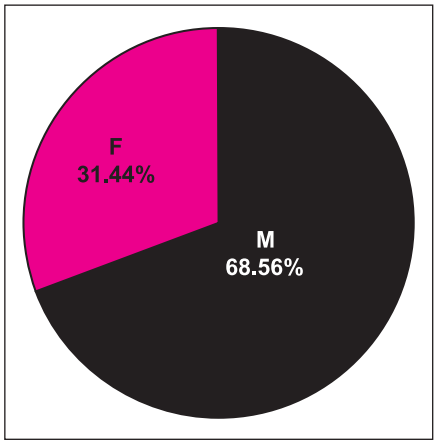

Figure 22. Percent distribution according to gender in RO-STEMI patients (M = males; F = females)

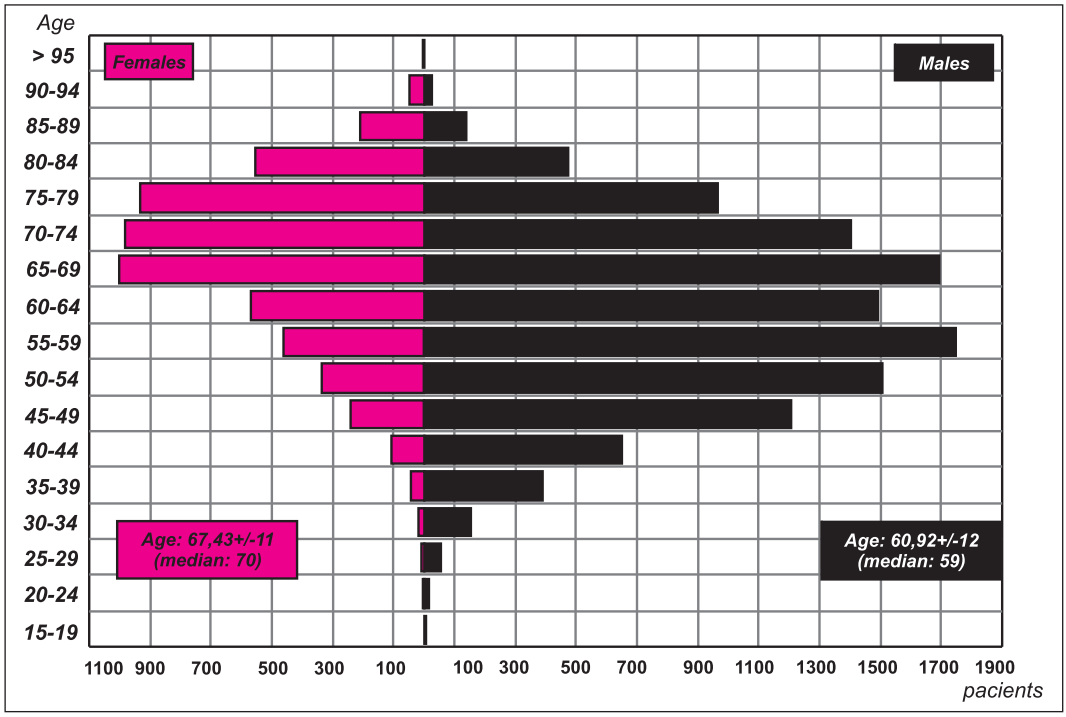

Figure 23. Distribution by age group and gender of RO-STEMI patients

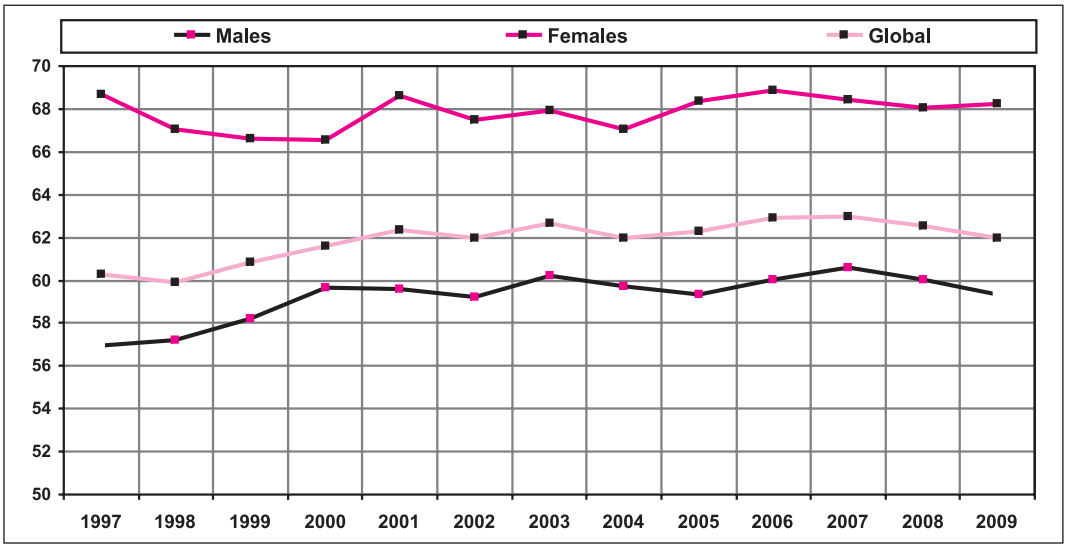

Figure 24. Mean age of RO-STEMI patients in the interval 1997 – 2009 (globally and by gender)

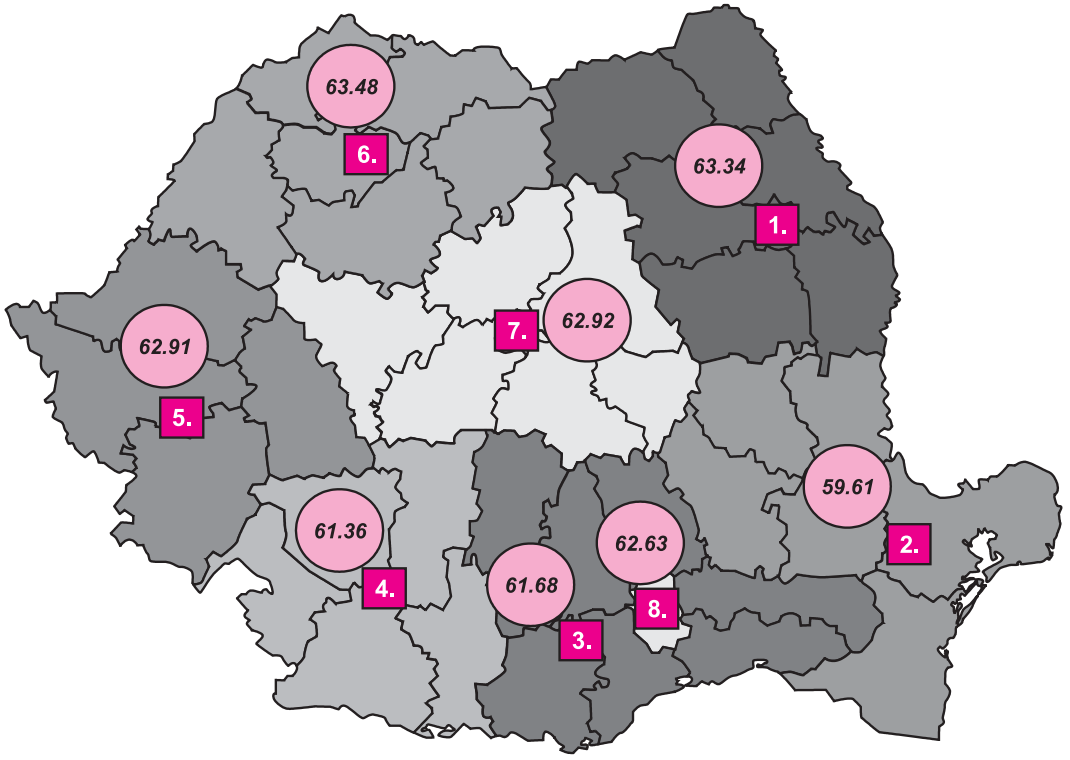

Figure 25. Romania's Development Regions and the mean age of RO-STEMI patients

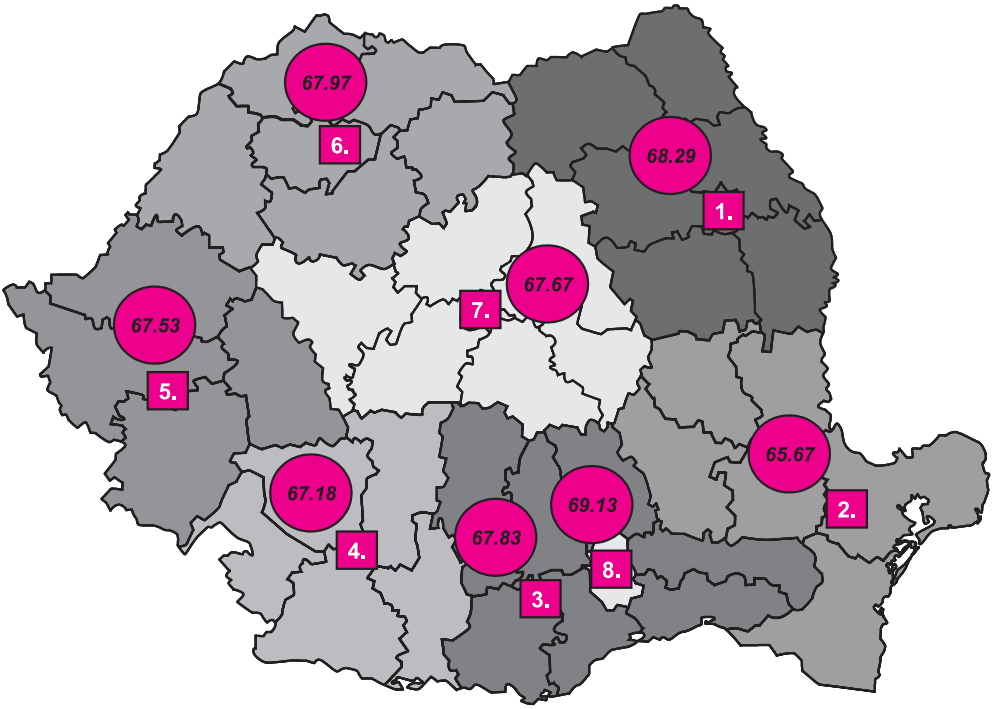

Figure 26. Romania's Development Regions and the mean age of female patients in the RO-STEMI registry

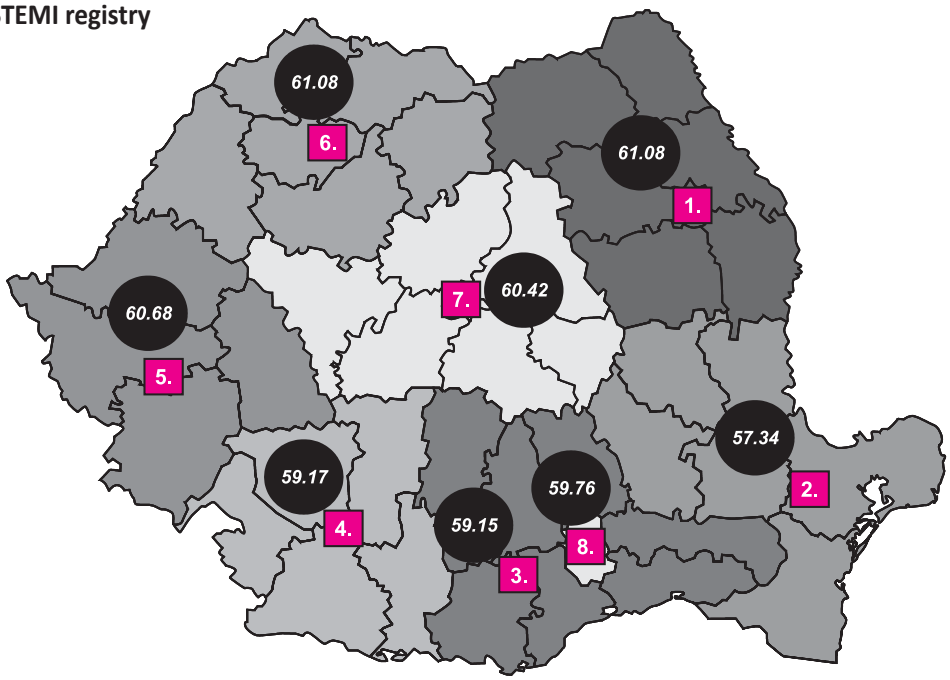

Figure 27. Romania's Development Regions and the mean age of male patients in the RO-STEMI registry

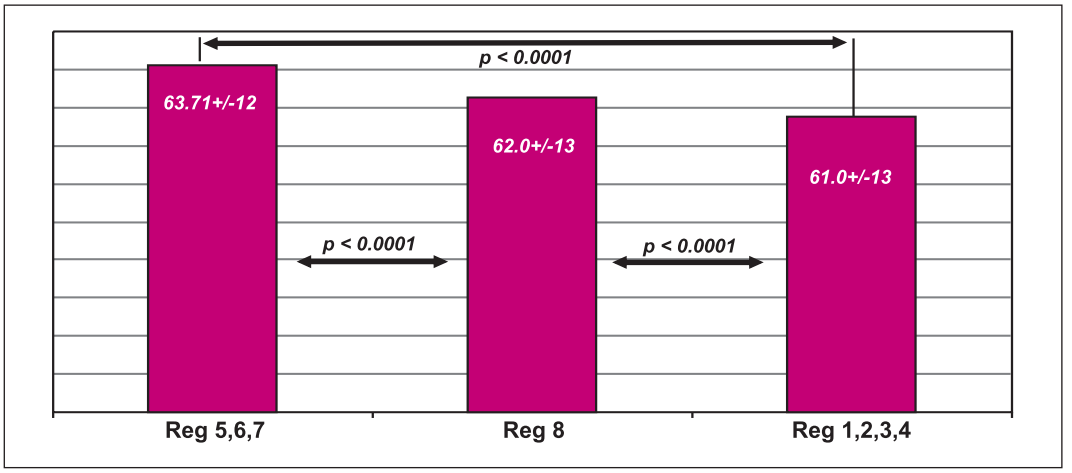

Figure 28. Differences between mean ages in RO-STEMI patients by per capita GNP in the different Development Regions (< 2800 Euro – Regions 1,2,3 and 4; between 2800 and 5600 Euro – Regions 5, 6 and 7; over 5600 Euro – Region 8)

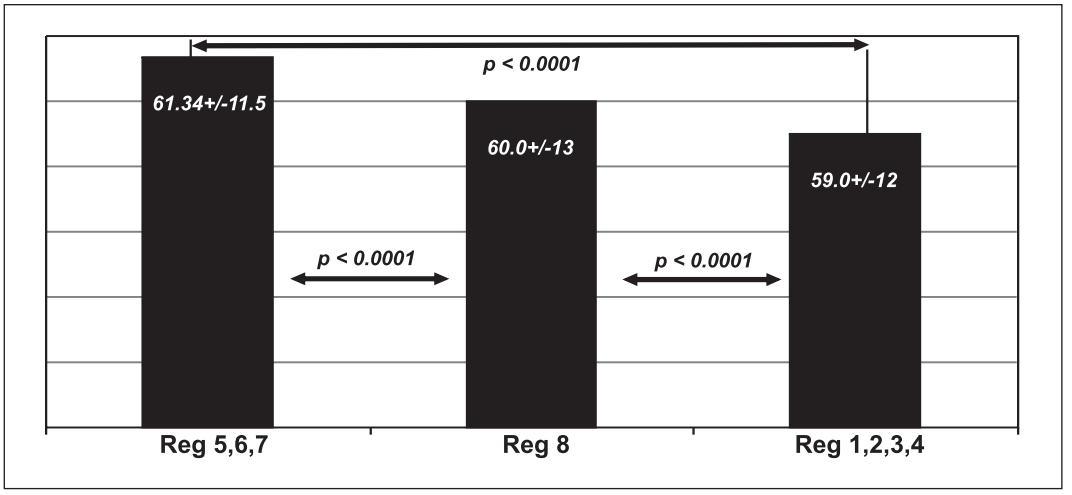

Figure 29. Differences between mean ages in male RO-STEMI patients by per capita GNP in the different Development Regions (< 2800 Euro – Regions 1,2,3 and 4; between 2800 and 5600 Euro – Regions 5, 6 and 7; over 5600 Euro – Region 8)

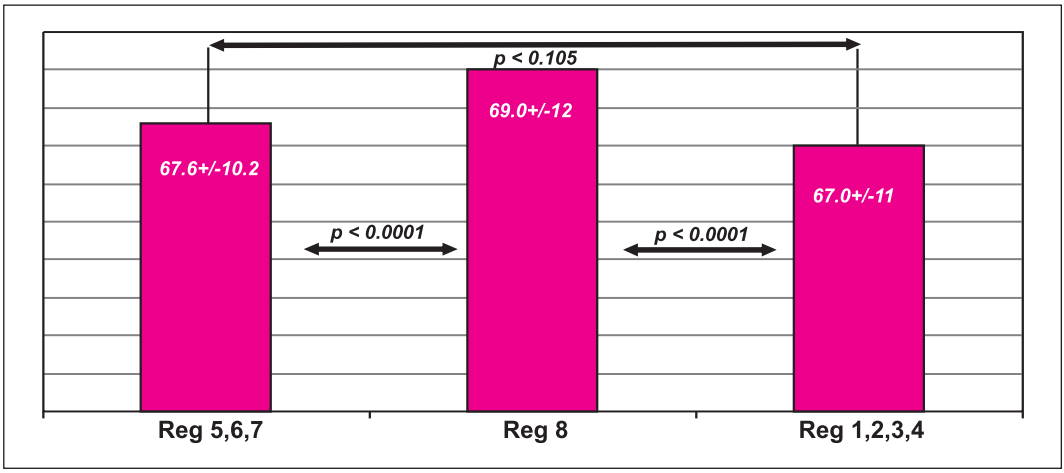

Figure 30. Differences between mean ages in female RO-STEMI patients by per capita GNP in the different Development Regions (< 2800 Euro – Regions 1,2,3 and 4; between 2800 and 5600 Euro – Regions 5, 6 and 7; over 5600 Euro – Region 8)

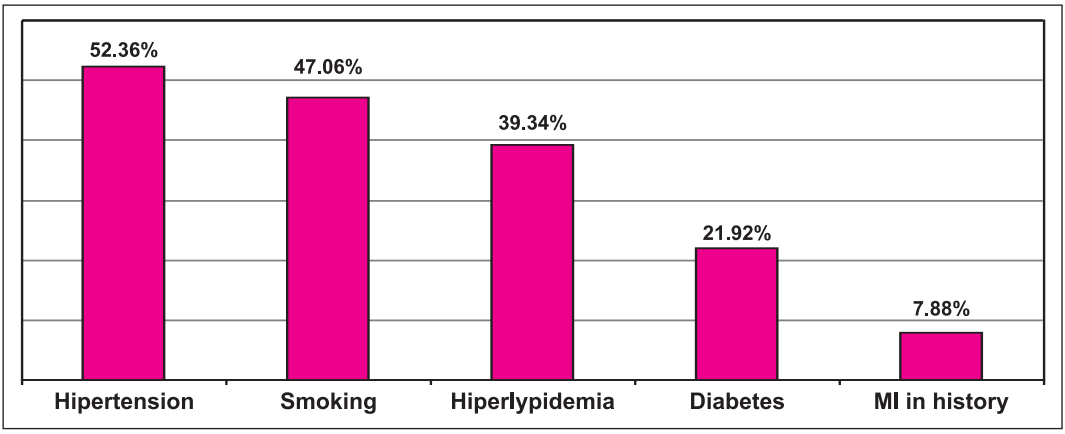

Figure 31. Percent distribution of the main coronary risk factors in RO-STEMI patients (MI = myocardial infarction)

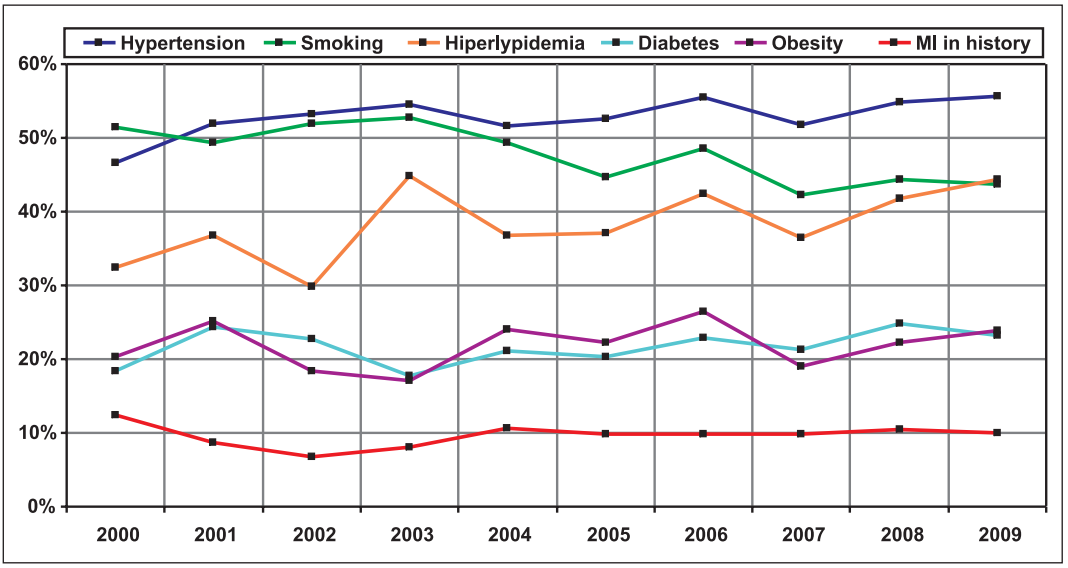

Figure 32. Incidence of the main coronary risk factors in RO-STEMI patients in the interval 2000 - 2009 (MI=myocardial infarction)

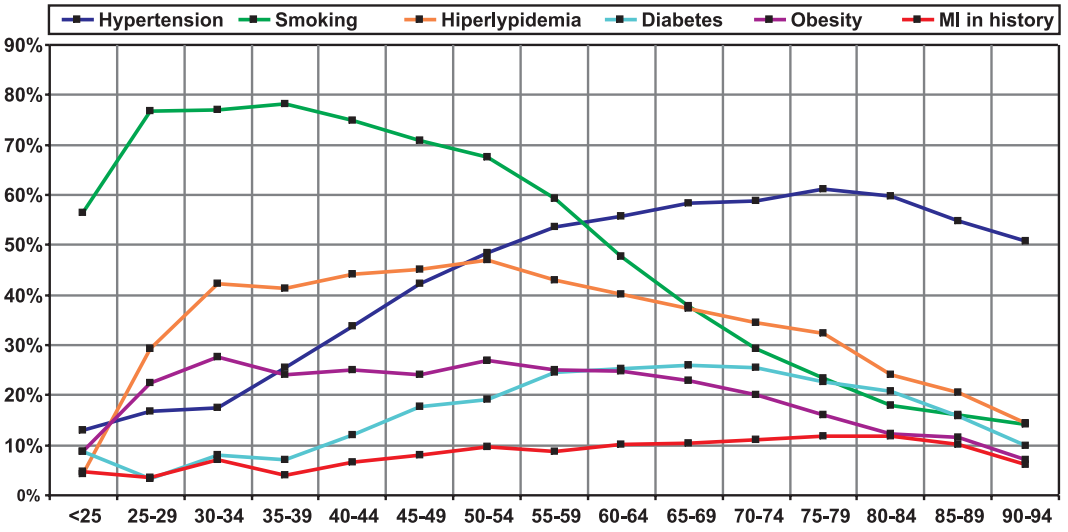

Figure 33. Percent distribution of the main coronary risk factors in RO-STEMI patients by age group (MI=myocardial infarction)

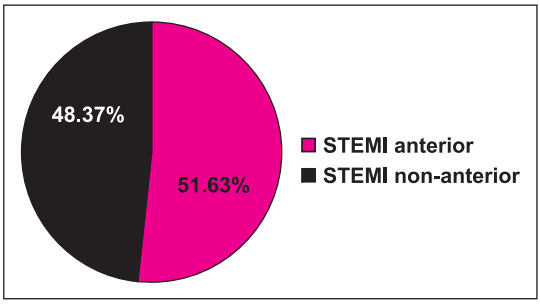

Figure 34. Percent distribution of RO-STEMI patients according to anterior vs. non-anterior infarct location

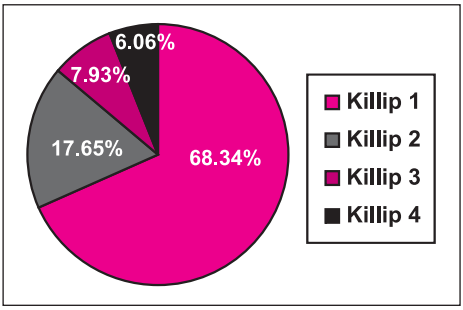

Figure 35. Percent distribution of 15191 RO-STEMI patients according to Killip class on admission

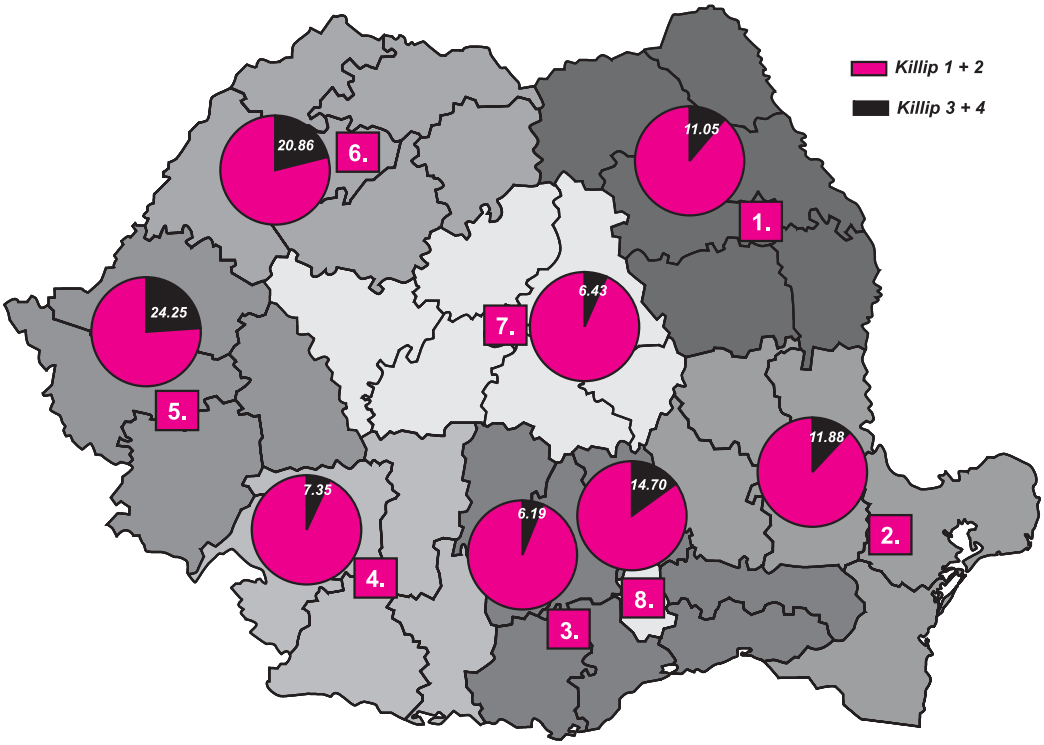

Figure 36. Percent distribution of 16693 RO-STEMI patients by Killip class on admission and by Development Region

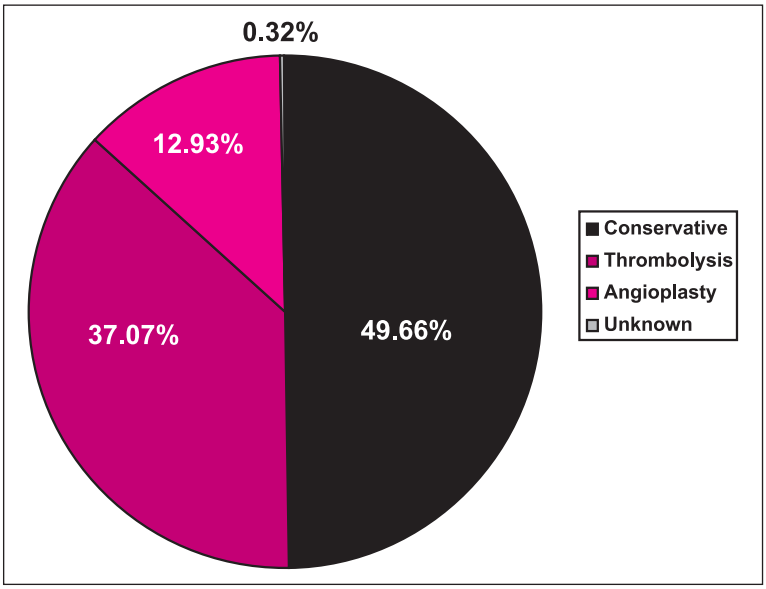

Figure 37. Type of treatment (reperfusion/conservative) in RO-STEMI patients

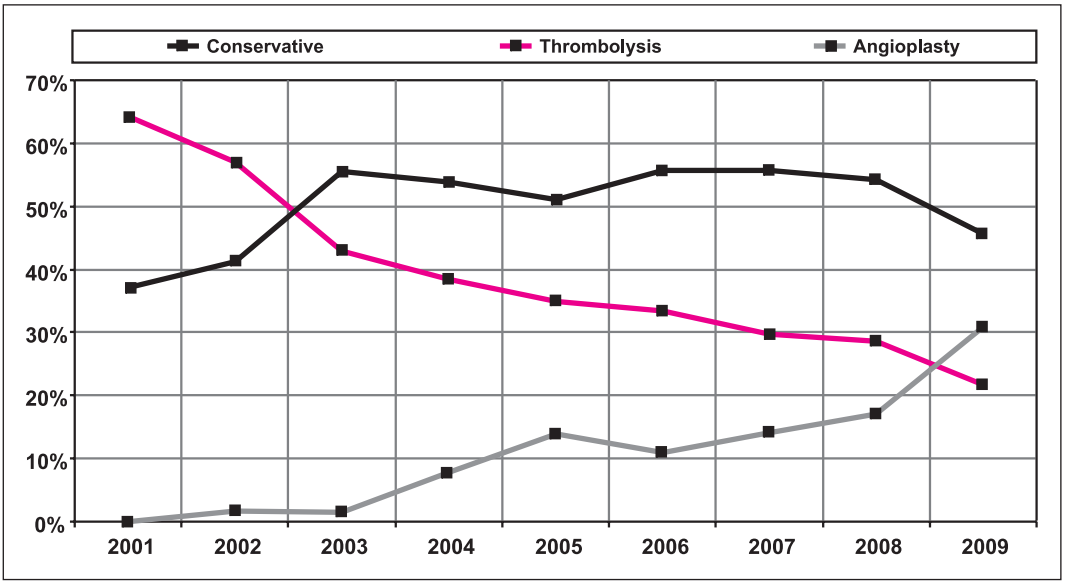

Figure 38. Percent distribution of RO-STEMI patients by therapeutic strategy (conservative vs. reperfusion therapy) in the interval 2001 - 2009

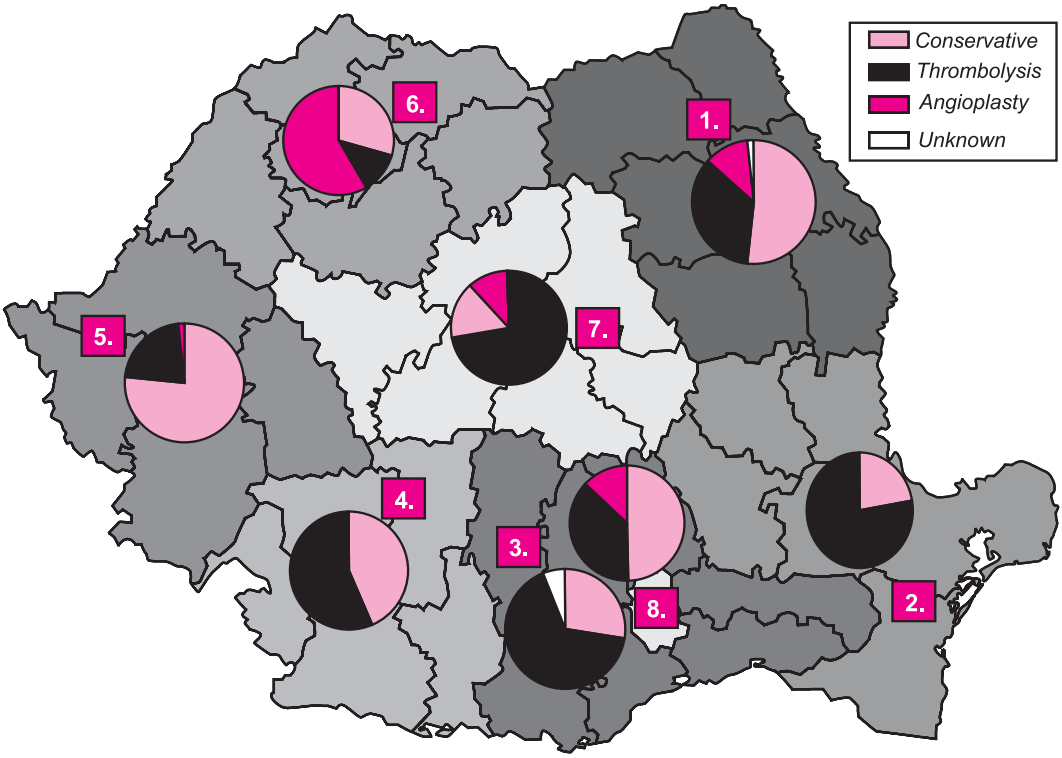

Figure 39. Percent distribution RO-STEMI patients by Development Region, according to type of therapy (conservative, thrombolysis, primary angioplasty)

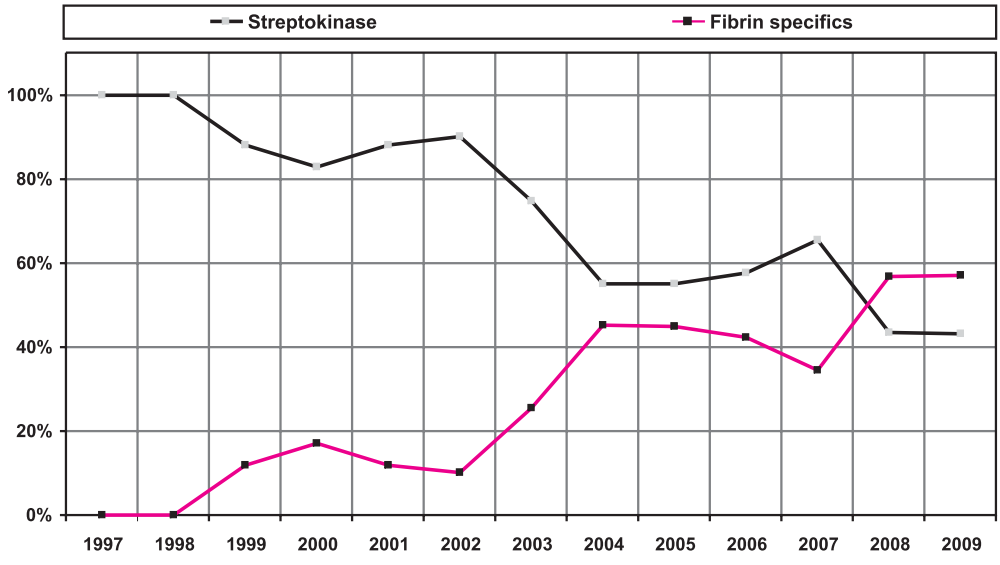

Figure 40. The utilization ratio of streptokinase vs. fibrin-specific fibrinolytics in fibrinolysed RO-STEMI patients in the interval 1997 - 2009

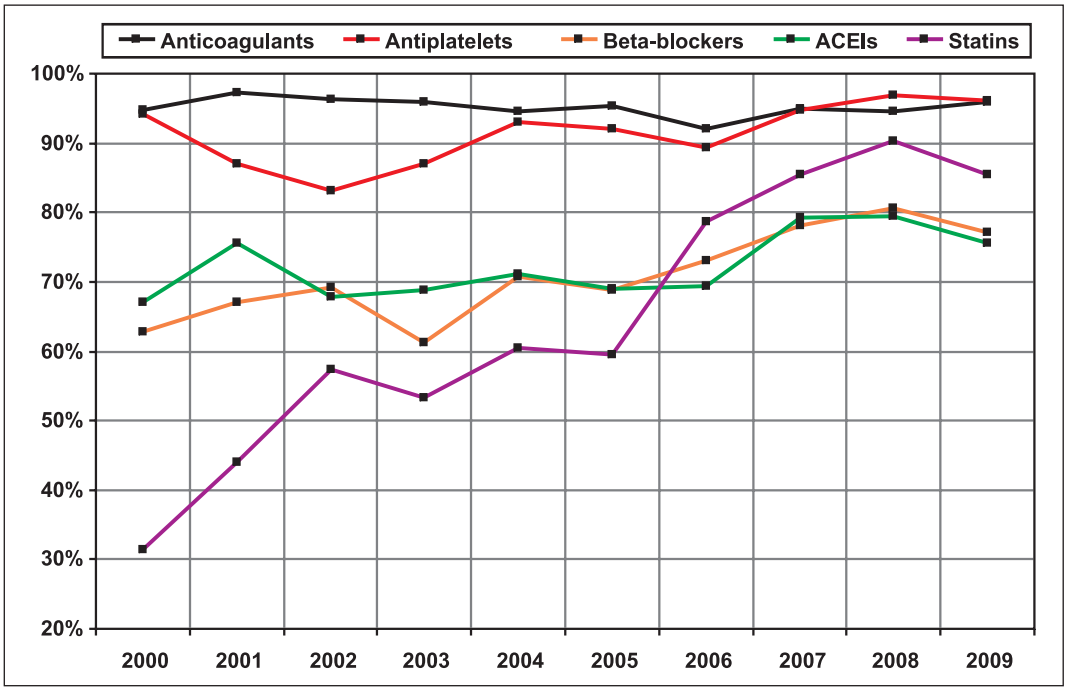

Figure 41. Evolution of the utilization rate of anticoagulants, antiplatelet agents, beta-blockers, ACE-inhibitors, and statins in RO-STEMI patients in the interval 2000 - 2009

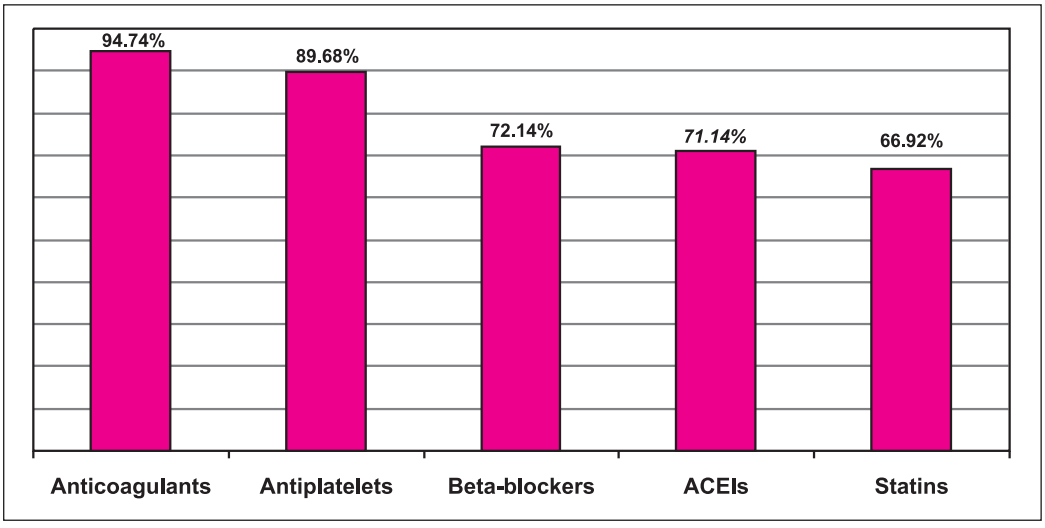

Figure 42. Global utilization rate of anticoagulants, antiplatelet agents, ACE-inhibitors, beta-blockers, and statins in RO-STEMI patients

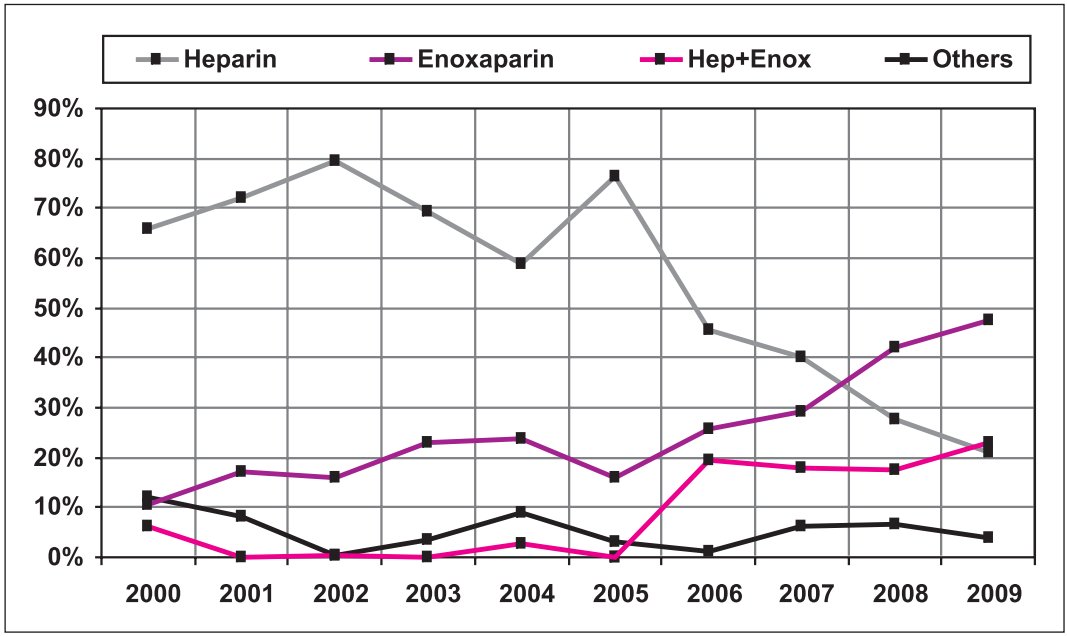

Figure 43. Changes in anticoagulant strategy in RO-STEMI patients in the interval 2000 - 2009

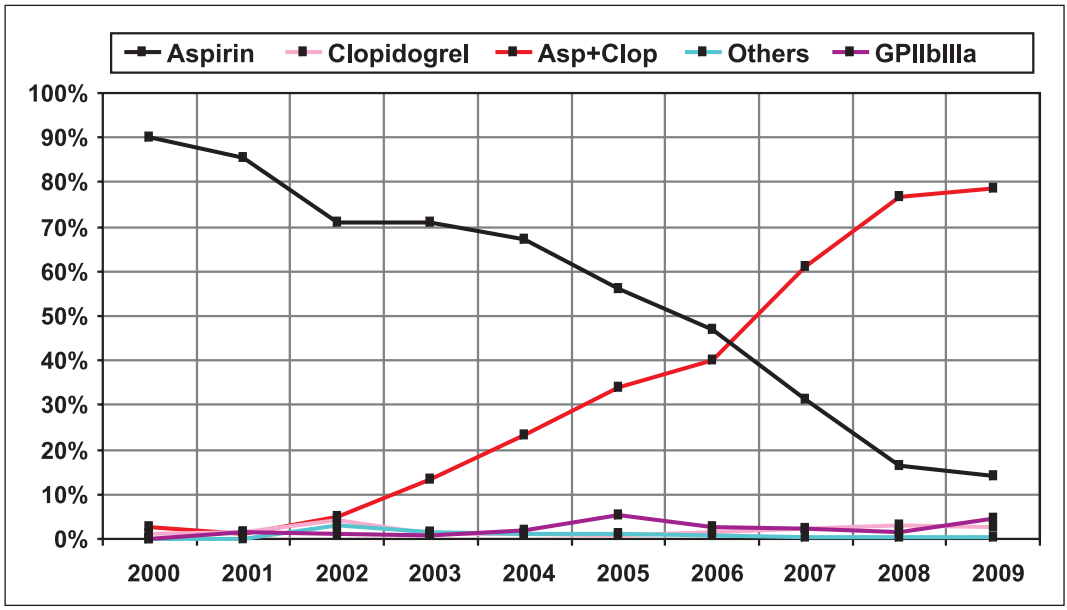

Figure 44. Changes in antiaggregation strategy in RO-STEMI patients in the interval 2000 - 2009

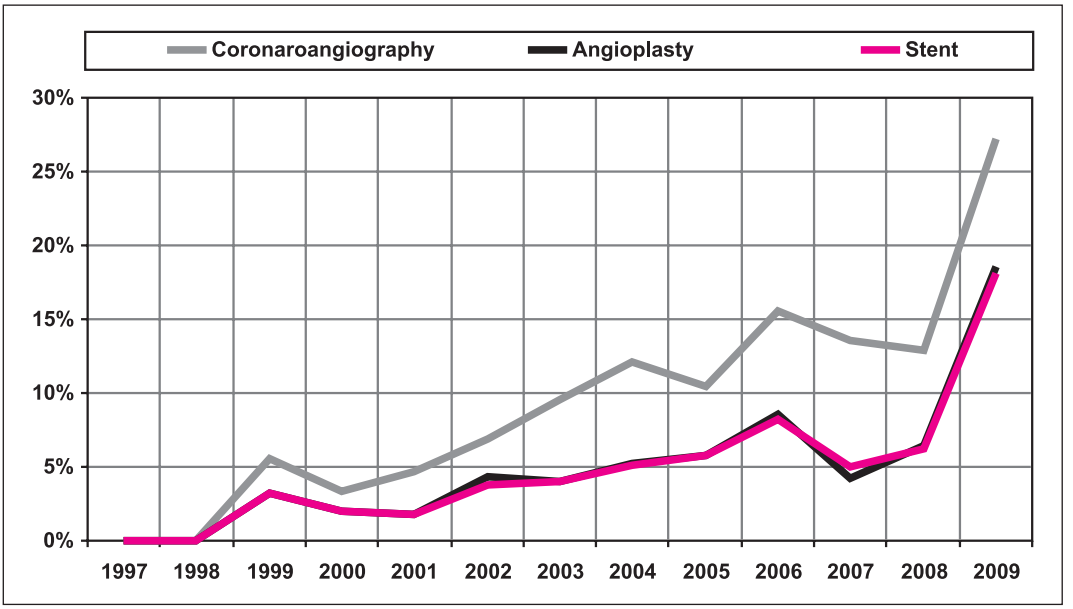

Figure 45. Yearly rate of angiography, angioplasty, and stent deployment in RO-STEMI patients treated conservatively or with thrombolytics

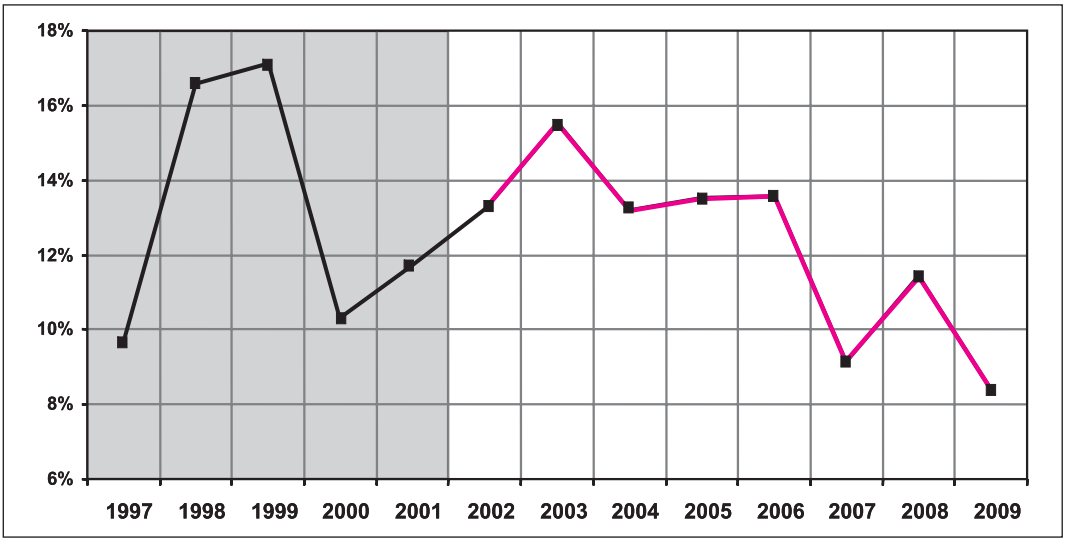

Figure 46. Yearly in-hospital mortality in RO-STEMI patients in the interval 1997 – 2009

(N.B. 1997 – 1998: only patients treated with thrombolytics, in 3 centers; 1999-2002 – over 50% patients treated with thrombolytics; 2003-2009 – balanced ratio between patients treated conservatively and those undergoing reperfusion)

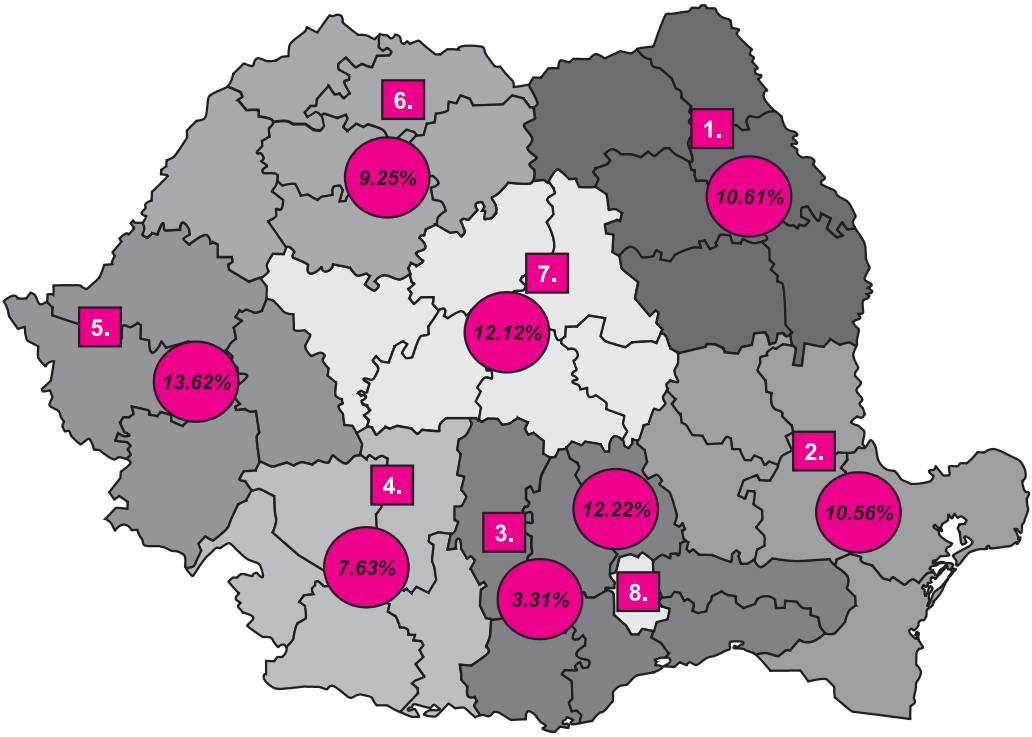

Figure 47. Global in-hospital mortality in RO-STEMI patients in the interval 1997 – 2009 by Development Region

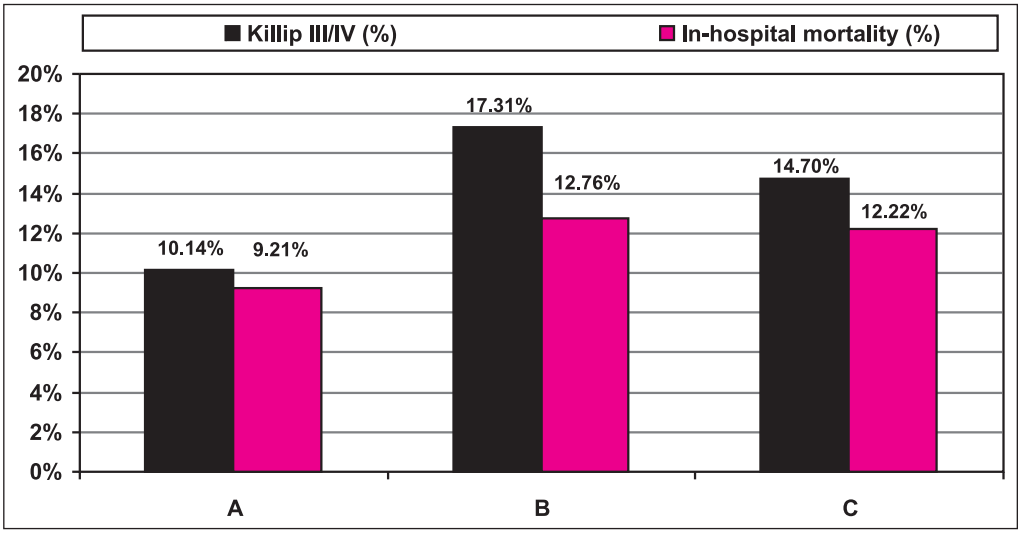

Figure 48. Proportion of RO-STEMI patients in Killip classes III and IV on admission and in-hospital mortality by Development Region:

A: per capita GNP< 2800 Euro (Regions 1,2,3,4); B: per capita GNP between 2800 and 5600 Euro (Regions 5,6,7); C: per capita GNP> 5600 Euro (Region 8)

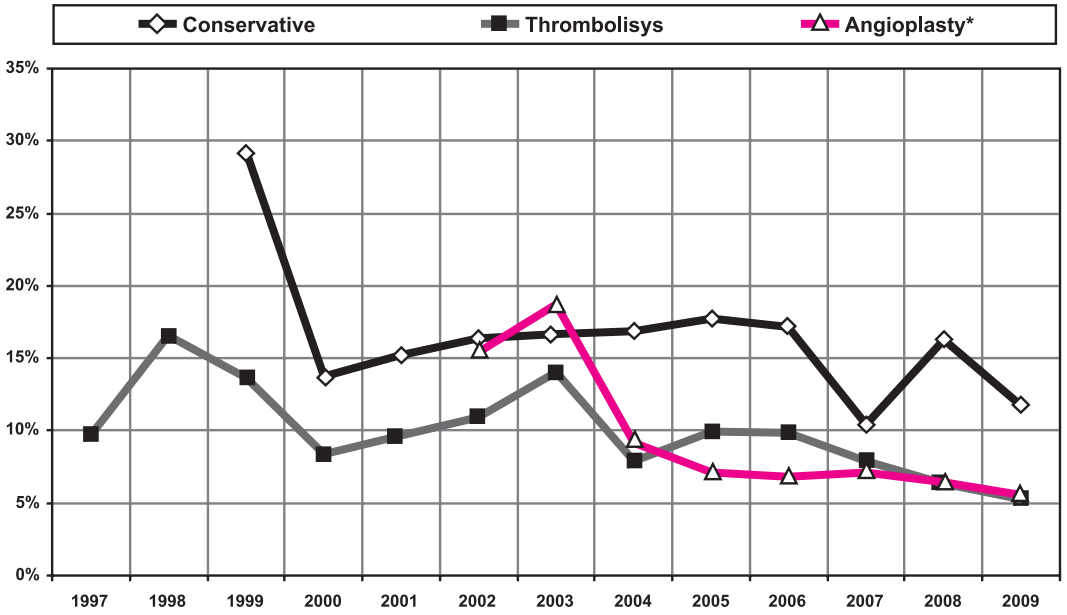

Figure 49. Yearly in-hospital mortality in RO-STEMI patients treated by thrombolytics, primary angioplasty, or conservative therapy, in the interval 1997 - 2009

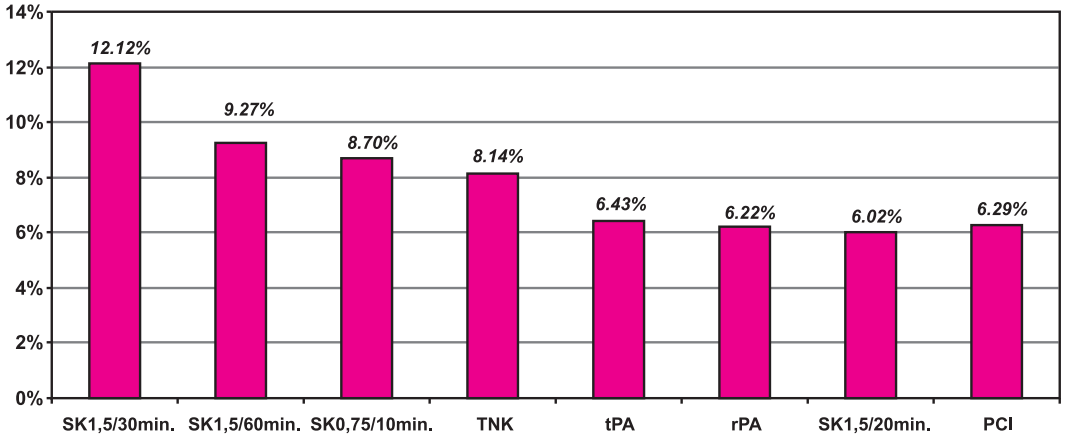

Figure 50. In-hospital mortality in RO-STEMI patients admitted in the interval 2005-2009 by type of reperfusion

(SK=Streptokinase; TNK=tenecteplase; tPA=alteplase; rPA=reteplase; PCI = primary angioplasty)

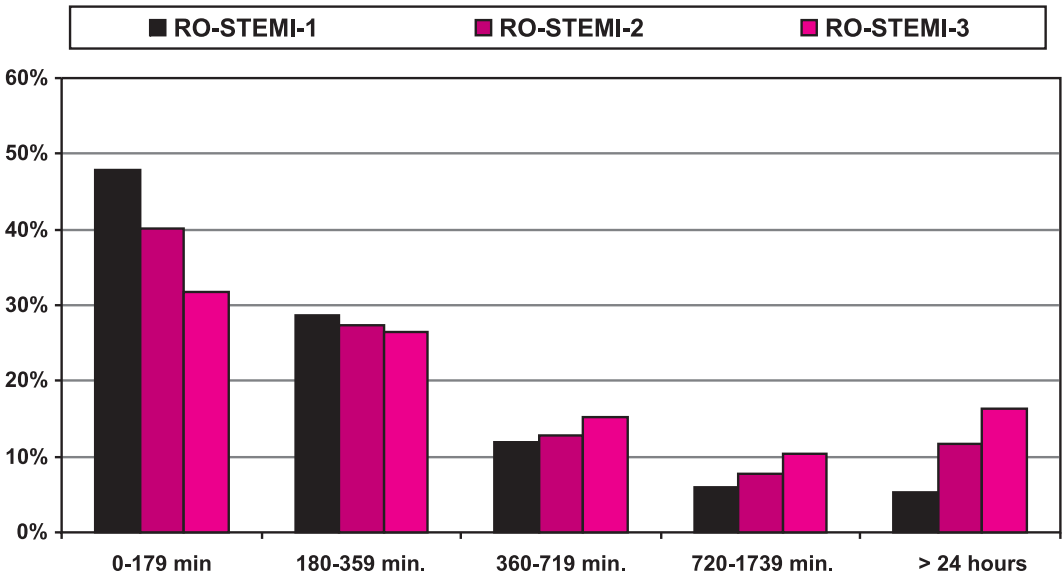

Figure 51. Percent distribution in 12507 RO-STEMI patients enrolled in the interval 1997-2001 (RO-STEMI-1), 2002-2005 (RO-STEMI-2) and 2006-2009 (RO-STEMI-3) by symptom onset-to-admission time

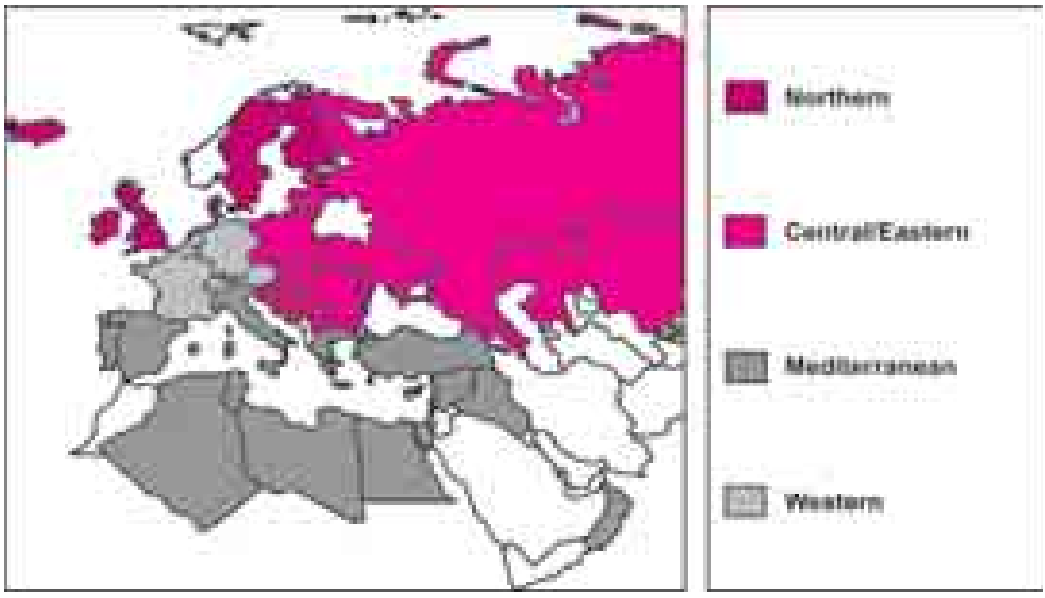

Figure 52. Participating countries in the EHS-ACS SNAPSHOT (2009) registry, by four geographical regions: Northern, Central and Eastern, Mediterranean, and Western countries

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