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## **REGIONAL CARDIAC NETWORK: THE EXPERIENCE AT THE EMERGENCY MEDICAL SERVICE 118 IN THE BASILICATA REGION IN ITALY**

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### **Abstract:**

*The aim of the regional cardiac networks is to offer to those patients affected by Acute Myocardial Infarction (AMI) the quickest and the most efficient treatment in relation to patients' characteristics and to the place where the event occurs. This article describes the experience developed by the Regional Emergency Medical Service of the Basilicata Region (Italy) in creating such a network. The structure of the network, the epidemiological data along with the different types of pathway used in the management of Non-ST elevation acute coronary syndromes are delineated with the aim to offer an overview of the clinical practices actually in place.*

*A retrospective observational study was conducted in 2012 with the aim to understand the incidence of AMI in its various forms: ST segment elevation myocardial infarction (STEMI) and Non-ST elevation acute coronary syndromes (NSTEMI).*

*The development of the Regional Cardiac Network has been shedding light on AMI and giving patients the chance to receive a customized treatment according to their clinical conditions. Further studies are recommended in order to understand the impact of these practices in terms of reduction of mortality and complications.*

### **Keywords:**

*Emergency Medical Services, Acute Myocardial Infarction, Non-ST Elevation Myocardial Infarction, Medical Treatment, Emergency Revascularization, Cardiovascular Network.*

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## **1. INTRODUCTION**

The aim of the regional cardiac networks is to offer to those patients affected by Acute Myocardial Infarction (AMI) the quickest and the most efficient treatment in relation to patients' characteristics and to the place where the event occurs. By perfecting the system of “warps and wefts” of the network and by making them smaller and more efficient, the negative impact represented by the regional topographic characteristics would be annulled or at least mitigated.

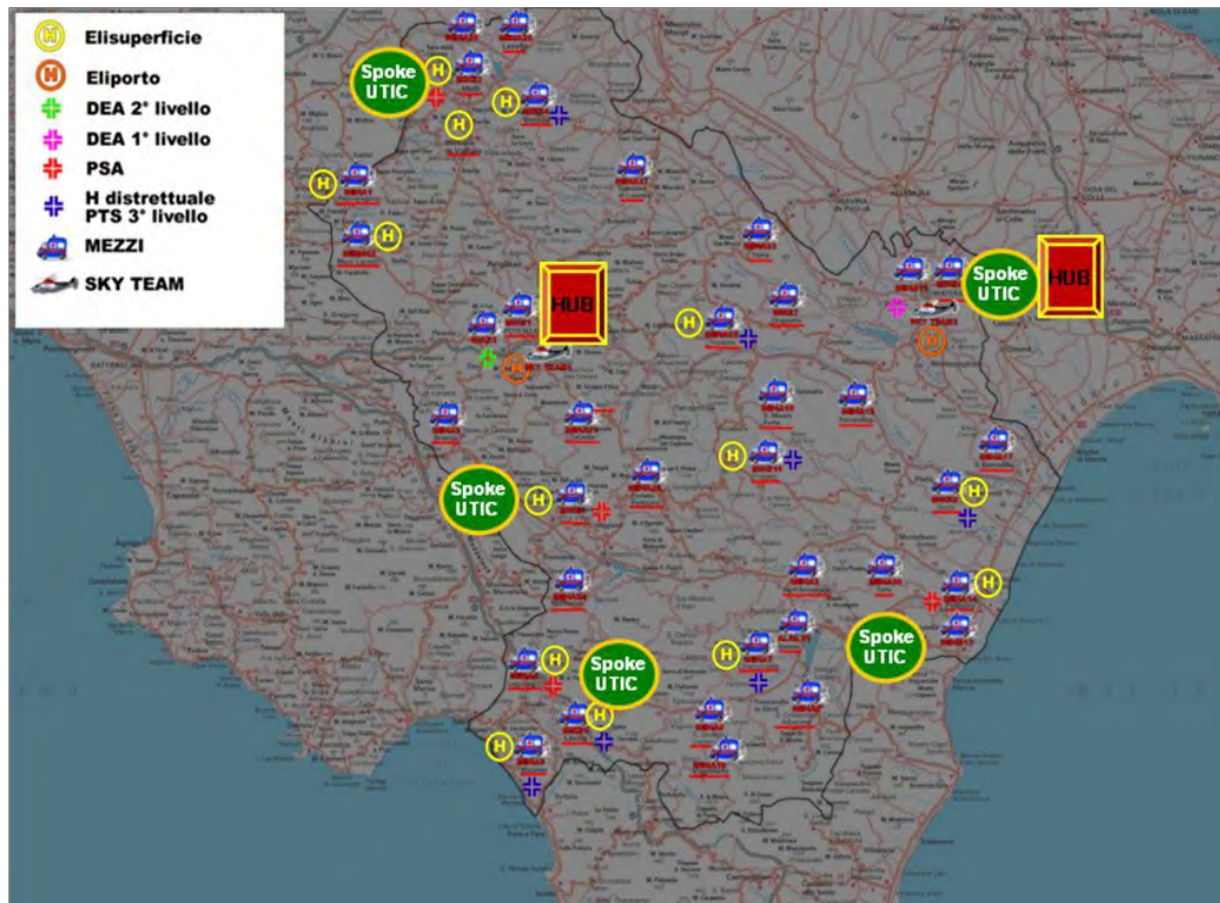


For instance, the Basilicata region, even if small, is characterized by a landscape of complex geography and by difficult road links which extend, very often, patients' waiting time of access to suitable hospitals, with the consequence of delaying the treatment.

In practical terms, this objective is realized by making an early and more efficient treatment for as many patients as possible, affected by AMI. Therefore, the optimal management of these patients entails the transformation of the traditional system of diagnosis and treatment, which is based on the concentration of all the medical procedures in one place only (Cardiac Intensive Care Unit-CICU of the nearest hospital from the place where the symptoms are manifested) and the procedures must be carried out but cardiology specialists. This transformation needs to happen in order to move towards a more complex system where the diagnosis, the risk stratification and the therapy of the first stages must be carried out in places that are not the CICU (Territory 118- Emergency) and by different health professionals (emergency doctors-territorial and hospital emergency) who work closely with the emergency community service headquarters 118 and the cardiologist working in the health care unit admitting the patient.

Such an organizational model becomes effective for all patients suffering from severe chest pain who call the emergency community service 118, which is able to perform a complete ECG in the place where this event occurs. In the Basilicata region all the 118 ambulances are equipped with a system of transmission of a complete 12 derivations ECG via telephone/GSM to reception stations within the emergency community service headquarters 118 and based in the CICU within the “San Carlo Hospital” in Potenza (regional HUB centre working 24 hours a day) and the “Madonna Delle Grazie Hospital” in Matera (HUB centre working 12 hours a day, since September 2012). The emergency community service 118 owns 34 ambulances, among which 25 non medicalised ambulances with nursing staff (India), and 9 medicalised ambulances (MIKE). To the above-mentioned 34 ambulances, a medical car and two helicopters must be added (only operating day flights).

There are four CICU structures (Spoke) in addition to the above-mentioned HUB centres, which are: Policoro, Villa D'Agri, Melfi, and Lagonegro.



As for the STEMI, where the diagnosis and therapeutic pathways are now validated, realised and generally used in the clinical practice, for the SCANTSE also an early diagnosis of the patient is fundamental for the early risk stratification, the treatment and to properly “guide” the patient.

It is therefore necessary to create a shared path in order to try to contextualise the recent ESC and ACC/AHA guidelines within the reality of the regional health care system.

## 2. EPIDEMIOLOGY

Cardiovascular diseases represent the main causes of mortality in the western world. In the last decade a reduction of mortality has been observed due to more efficient medical and surgical treatments. Despite this fact, morbidity and mortality rates have increased in Eastern Europe and in Africa due to the typical life style of industrialised countries.<sup>1</sup>

The real natural story and the epidemiological impact of AMI are still difficult to assess for several reasons: the frequent development of a silent AMI, the occurrence in many cases of mortal prehospital events and the different ways of classifying these events.



In the last years the intrahospital mortality for AMI has reduced, going from 25%-30% during the 60's to 18% in the 80's until reaching around 10% in the last clinical trials. On the contrary, though, prehospital mortality has not diminished.

Patients with NSTEMI (generally with an underdevelopment of ST segment or with an inversion of T waves, but also with a ECG without significant alterations) are older, they are exposed to a higher coronary risk, they have a longer history of coronary disease, with a higher prevalence of previous AMI, angioplasty, aortocoronary bypass and events of heart failure.<sup>3-4</sup>

Furthermore, coronary disease tend to be more widespread in patients with NSTEMI, in whom the prognostic impact of a myocardial damage, even if minor, is definitely higher.<sup>5-6</sup>

For this reason the long-term prognosis of NSTEMI is generally and usually more serious than the presentations with STEMI, even if the hospital stay is more beneficial in comparison with patients with STEMI.<sup>1-2-4</sup>

The epidemiological data of the last years indicate a clear trend towards a continuous increase of hospital admissions for NSTEMI compared to those for STEMI.<sup>1-2</sup>

In the BLITZ 3 study, which registered 6,986 consecutive hospital admissions, in 332 UTIC in 2008, 59% of admissions for AMI was due to NSTEMI (form). A study carried out in three Italian regions (Emilia Romagna, Lombardia, Friuli Venezia Giulia) between 2001 and 2005 highlighted how STEMI had a reduction from 19,733 to 17, 574 while NSTEMI have more than doubled raging from 6,194 to 12, 951.<sup>8</sup>

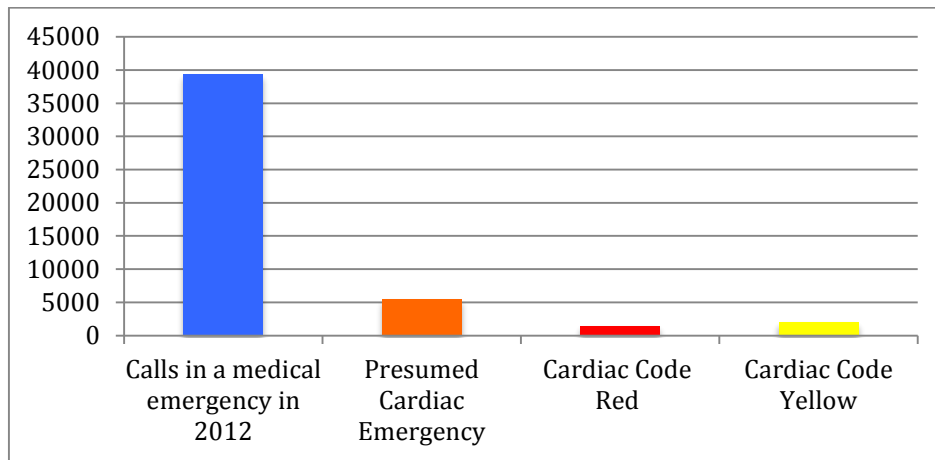
At the time of the admission, NSTEMI present a minor risk of premature events compared to STEMI. Then, when they affect individuals with a higher risk profile, they lose with time much of their prognostic initial advantage over the STEMI one, so much that within 4 years even mortality due to NSTEMI is double.<sup>9</sup>

Age and place of treatment not only determine the differences in the events for patients with SCA but also differences in therapies. Only one third of older patients has, in fact, the possibility of receiving the adequate treatment in a cardiology ward, independently from the diagnosis of STEMI or NSTEMI.

In general only one in ten patients who have not been treated in a cardiology ward, undergoes a coronarography or a revascularization procedure.

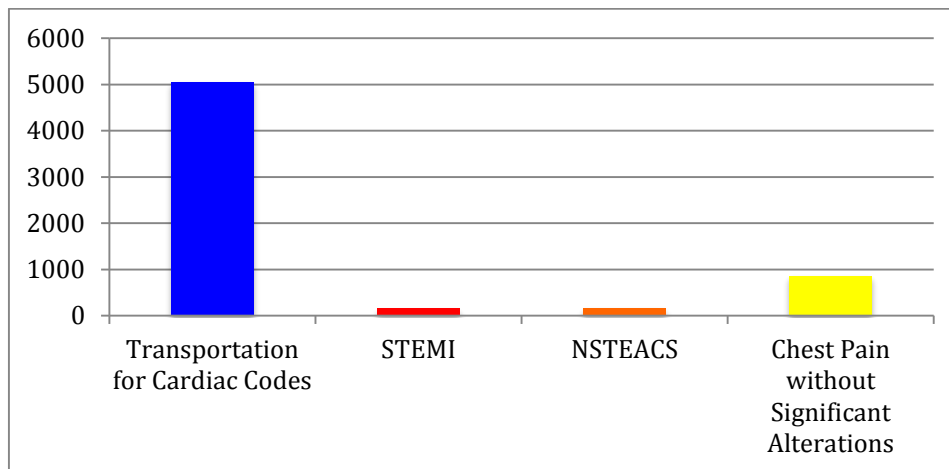
### Data collected in 2012 in Basilicata Region

Ambulance Dispatch	<b>Calls in a medical emergency in 2012</b>	<b>39,318</b>
	<b>Presumed Cardiac Emergency</b>	<b>5,478</b>
	<b>Cardiac Code Red</b>	<b>1,477</b>
	<b>Cardiac Code Yellow</b>	<b>3,740</b>



Ambulance Transportation to Hospital

Transportation for Cardiac Codes	Count
STEMI	160
NSTEACS	164
Chest Pain without Significant Alterations	869



### 3. NETWORK FOR NSTEMACS TREATMENTS

It is now recognised that the NSTEMACS have medium term diagnosis which is not very different from the STEMI one.

This makes necessary the optimal use of resources in the most serious cases, which require an invasive strategy, even when these are initially received in centres which lack in hemodynamics.



Those patients diagnosed as high/medium risk benefit from an early aggressive treatment (coronography and revascularization in a short time) with a significant reduction of mortality and of AMI at a five-year follow-up. For the low risk patients, none of the studies comparing a conservative strategy to an early invasive one, have highlighted any advantage of an early invasive strategy.<sup>10</sup>

Consequently, it appears evident that the necessity is to properly address the use of resources giving priority to the high-risk patients through the implementation of shared algorithms between territory and hospital (Spoke and Hub) with the purpose of:

- Performing a correct evaluation of chest pain and of the different degrees of NSTEMI severity;
- Directing the patients affected by high risk NSTEMI to intensive care units with hemodynamics;
- Ensuring the appropriateness of pharmacological treatments;
- Raising the percentage of high risk patients who would be promptly treated with a surgical therapy;
- Carrying out adequate treatments for all patients, independently from the place where the diagnosis is performed, through the activation of the cardiology network;
- Ensuring an adequate assistance even in the post acute phase, after discharge.

The new guidelines of the European Society of Cardiology (ESC)<sup>11</sup> advise a global prognostical evaluation based on the combination of the following criteria:<sup>12</sup>

- Clinical anamnesis
- Symptoms
- ECG
- Biochemical markers
- Score of clinical risk

The most used score of clinical risk are TIMI RISK SCORE and GRACE RISK SCORE.

TIMI is a simple tool that uses seven risk indicators at admission. Each score is associated with a specific risk of poor outcome such as death, heart attack, myocardial infarction and emergency revascularization.



## TIMI RISK SCORE for UA/NSTEMI

HISTORICAL	POINTS	RISK OF CARDIAC EVENTS (%) BY 14 DAYS IN TIMI 11B*		
		RISK SCORE	DEATH OR MI	DEATH, MI OR URGENT REVASC
Age $\geq 65$	1	0/1 2 3 4 5 6/7	3 3 5 7 12 19	5 8 13 20 26 41
$\geq 3$ CAD risk factors (FHx, HTN, $\uparrow$ chol, DM, active smoker)	1			
Known CAD (stenosis $\geq 50\%$ )	1			
ASA use in past 7 days	1			
<b>PRESENTATION</b>				
Recent ( $\leq 24$ H) severe angina	1			
$\uparrow$ cardiac markers	1			
ST deviation $\geq 0.5$ mm	1			
<b>RISK SCORE = Total Points (0 – 7)</b>				

\*Entry criteria: UA or NSTEMI defined as ischemic pain at rest within past 24H, with evidence of CAD (ST segment deviation or  $\uparrow$ marker)

For more info go to [www.timi.org](http://www.timi.org)

Antman et al JAMA 2000; 284: 835 - 842

The GRACE RISK SCORE was developed through the multivariate analysis from a population of 11,389 patients affected by AMI of the GRACE register; the possibility of predicting the variables was validated on 3,962 patients of the GRACE and on 12,142 patients of the GUSTO-II b.

In this case, these are predictive variables of intrahospital mortality within 6 months, to which a partial score, in calculating the global score, is attributed.<sup>13-14</sup> The variables considered for predicting the intrahospital mortality, based on the characteristics of prevalence of NSTEMI at admission, are of course the ones which are most relevant in choosing a treatment strategy:

- Killip class
- Age
- Systolic arterial pressure
- Cardiac frequency
- Creatinine levels
- Cardiac arrest
- Deviation of the ST segment
- Troponin increase

Therefore, three categories of patients with a different risk profile are identified at admission with a different timing for the execution of the coronagraphy<sup>18-19</sup> (the early invasive treatment should be proportionate to the level of basal risk).





## 1- URGENT CORONOGRAPHY

The patient who is affected by persistent angor or recurrent angina pectoris or showing signs of heart failure, hypotension (PA<100mmHg) or with ventricular arrhythmia which are potentially lethal has to be taken to the HUB centre (might he be on the territory or in spoke hospital) by calling 118 (by helicopter or ambulance), activating this way the cardiac network, as for the STEMI.

## 2- CORONOGRAPHY WITHIN 24 HOURS

Patients with a high score of clinical risk (GRACE>140 with intrahospital mortality>3%) or showing three or more risk variables: 75 year of age or older, killip class>1, diabetes mellitus, increase of troponin at admission, systolic arterial pressure<100 mmHg have to be directed to the HUB centre of reference in order to perform an invasive study within 24 hours.

## 3- CORONAROGRAPHY WITHIN 72 HOURS

Patients with medium risk (GRACE score 109-140, intrahospital mortality 1-3 %);

## 4- ARRANGEABLE CORONAROGRAPHY

Patients with complete regression of symptoms, in medical therapy ad hoc, in the absence of signs of cardiac insufficiency, of anomalies during the first ECG and the ones after (within 6 or twelve hours) and in the absence of an increase in the troponin levels (at admission and within six or twelve hours) or with a low GRACE score (1-108; mortality<1%).

## 5- NO INDICATION DURING CORONAROGRAPHY (either early or elective)

in patients considered globally weak, very compromised due to severe comorbidity, who are not physically autonomous, due to severe disease such as multi infarct encephalopathy, or affected by severe respiratory insufficiency, renal insufficiency with creatinine clearance<30ml/min, chronic severe hepatopathy, with severe anemia (hb<10 gr/dl) and sever spontaneous hemorrhagic risk.

These are patients with a very low life expectancy, for whom the stress resulting from an invasive examination and mainly from performing a contrast procedure could be more damaging than useful.<sup>16</sup>

GRACE Risk Score - Total possible score is 258

Age (years)	Score
<40	0
40 – 49	8



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50 – 59	36
60 – 69	55
70 – 79	73
≥80	91

Heart rate (bpm)	Score
<70	0
70 – 89	7
90 – 109	13
110 – 149	23
150 – 199	36
>200	46

Systolic BP (mmHg)	Score
80	63
90 – 99	58
100 – 119	47
120 – 139	37
140 – 159	26
160 – 199	11
>200 = 0	0

Creatinine (mg/dL)	Score
0.0 – 0.39	2
0.4 – 0.79	5
0.8 – 1.19	8
1.2 – 1.59	11
1.6 – 1.99	14
2.0 – 3.99	23
>4	31

Killip class	Score
Class I	0
Class II	21
Class III	43
Class IV	64

Cardiac arrest at admission:	43
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Elevated cardiac markers:	15
ST segment deviation:	30

#### 4. PHARMACOLOGICAL THERAPY

On the territory and in the DEA the NSTEMI runs in parallel with the clinical and anamnestic evaluation and with diagnostic tests.

The ACC/AHA advises the appropriate therapy on the basis of risk stratification and clinical risk.<sup>20</sup>

The treatment strategy is based on four categories of drugs:

- Anti ischemic therapy
- Reperfusion therapy
- Antiplatelet therapy
- Anticoagulation therapy

Reperfusion therapy is taken in consideration from the beginning of the process, since the decision of treating the patient with an invasive or a conservative approach influences both the anticoagulation and the antiplatelet therapy.

The anti ischemic therapy for those patients affected by NSTEMI should focus on the unbalance between demand and offer of oxygen within the myocardial cells.

This therapy begins with resting in bed, having supplemental oxygen (when indicated) and it continues with the administration of nitro derivatives (when the hemodynamic status and the place of IMA allow it).

The most recent guidelines recommend the use of oral beta-blockers in those patients that don't have any side effects, only though in the first 24 hours from their arrival in DEA.

Morphine sulphate is used as an anti ischemic therapy in those patients affected by pain, which is resistant to nitro derivatives.

**Antiplatelet therapy** is essential due to the active nature of coronary thrombus and to the role that platelet aggregation has in these patients. Once the diagnosis has been performed, such therapy needs to be undertaken as soon as possible in order to reduce both the risk of acute ischemic complications and of recurrent thrombotic episodes. Platelet inhibition derives from three categories of drugs, each having its own specific action mechanism:

- Aspirin



- P2Y receptor inhibitor
- Glycoprotein IIb/IIIa inhibitors

A dose of aspirin of 150-300 mg, is effective in reducing the consequences of a reoccurring heart attack and the mortality in those patients affected by NSTEMI.

P2Y receptor inhibitors are:

- CLOPIDOGREL
- PRASUGREL
- TICAGRELOR12

The efficiency of CLOPIDOGREL administration (oral dose of 300mg followed by 75 mg) together with the aspirin has been demonstrated in the “CURE” study. The positive effect was significative mainly in those patients undergoing an angioplasty. The risk reduction is significative for AMI with a tendency towards cardiovascular mortality reduction for stroke episodes. Following aspirin intake interruption, a rebound effect is manifested especially in those patients treated with a conservative therapy. Patients treated with CLOPIDOGREL also face consequences of a higher possibility of major hemorrhagic episodes with a significant increase of fatal bleeding.

PRASUGREL and TICAGRELOR represent the new antiaggregant drugs. PRASUGREL is a thienopyridine of third generation and as CLOPIDOGREL is a prodrug that needs hepatic metabolism for its activation.

The study of TRITON-TIMI 38 compared PRASUGREL (a dose of 60mg followed by 10mg/die) to CLOPIDOGREL in patients who will undergo a Percutaneous Coronary Intervention (PCI) for NSTEMACS with a medium and high risk. There were no observable differences concerning the occurrence of non fatal strokes and cardiovascular mortality, while in the whole studied population, the occurrence of STENT thrombosis resulted significantly lower in the group treated with PRASUGREL compared to the group treated with CLOPIDOGREL. In those patients treated with PRASUGREL there was an increase of bleeding rate.

Furthermore, for patients older than 75 and for patients with a body weight lower than 60 Kg there was not a real clinical benefit; instead in diabetic patients there was a higher benefit not associated with an increase of hemorrhagic risk.<sup>17</sup>

TRICAGRELOR, oral reversible inhibitor of the platelet receptor P2Y<sub>12</sub>, has a quicker and constant action compared to CLOPIDOGREL, however its effects are more rapidly reversible, allowing a quicker recovery of platelet function.

TRICAGRELOR (at a dose of 180mg) has resulted associated to a reduction of STENT thrombosis occurrence, with a reduction of myocardial heart attack episodes and with a reduction of mortality (even if the last two results were shown in a period of time of 12 months of the treatment).



TRICAGRELOR also resulted associated to a reduction of early and late mortality post Coronary Artery Bypass Grafting (CABG).

However the TRICAGRELOR side effects must be taken in consideration, such as dyspnea and a higher frequency of ventricular poses and an increase of the occurrence of minor bleeding episodes.

The IIb/IIIa glycoprotein inhibitors have a favorable significant effect especially when they are administered during PCI.

The anticoagulation therapy is performed during NSTEMACS with the purpose of inhibit the production and/or the thrombin activity with a consecutive reduction of thrombus formation correlated events.

The association of anti-platelet and anticoagulation therapies is more effective than the isolated administration of these two categories of drugs.

In regards to NSTEMACS, coagulation indirect as well as direct inhibitors have been considered. In patients affected by NSTEMACS, EBPM doses are adjusted according to their body weight and they are subcutaneously administered every 12 hours, however a first intravenous bolus is performed for those high-risk patients.

FONDAPARINUX (2,5 mg-die) has an anticoagulation effect about 50% lower than ENOXAPARINA at standard doses (1 mg per Kg twice a day) and its inhibitory action on thrombin is two times less than the action of ENOXAPARINA.

The low levels of anticoagulation, if on one side prove the significant reduction of haemorrhagic risk, on the other side they are not sufficiently adequate to prevent catheter thrombosis episodes during PCI, therefore confirming the necessity of an additional Unfractionated Heparin bolus, during the treatment in those patients previously pretreated with FONDAPARINUX.

Unfractionated Heparin has a narrow therapeutic window, therefore continual Partial Thromboplastin Time (PTT) monitoring is required. Adjusted doses of Unfractionated Heparin according to body weight are recommended, with a first bolus of 60-70 UI/KG up to a maximum of 5000UI followed by an infusion of 12-15UI/Kg up to a maximum of 1000UI.

## **5. NSTEMACS PATHWAY**

The organisation of the Cardiac Network for Non-ST elevation myocardial infarction is based on recommendations expressed in the guidelines provided by the European Society of Cardiology, published in the European Heart Journal on the 21st of September 2011.

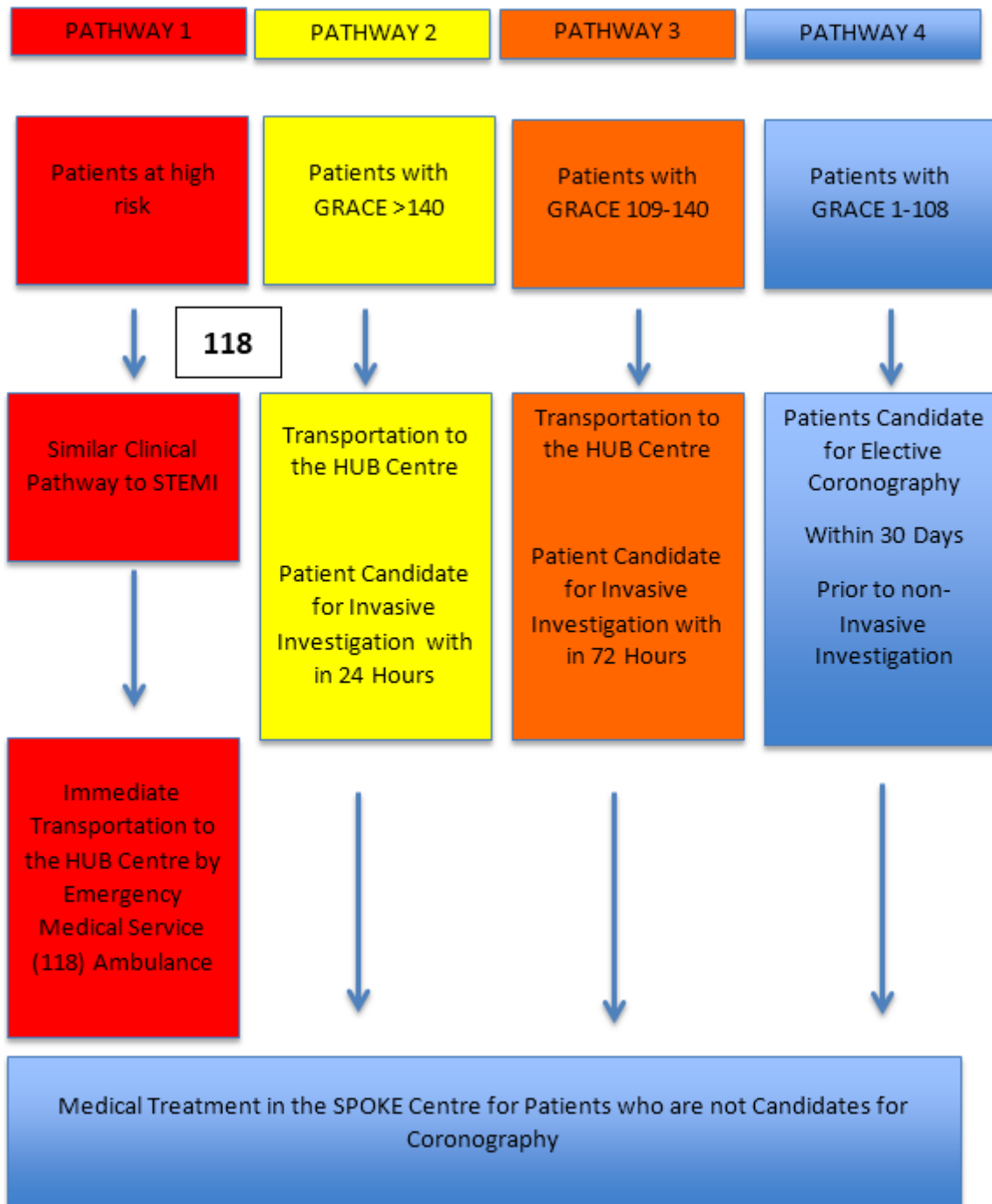


Patients with thoracic pain or with equivalent symptoms, who are in their home or have been succored by the 118 emergency team, must be checked from a clinical, anamnestic and instrumental point of view (12 derivations ECG).

In case of positive ECG showing alterations of either ST segment or T and therefore compatible with NSEACS and with cardiac failure, hypotension or hemodynamic or electric instability, the doctor working for the emergency 118, after a phone consultation with the accepting cardiologist (who in turns will have received all the clinical information about the patient and will have seen the ECG), will have to take the patient directly to the HUB centre for an urgent coronography. Patients with a typical thoracic pain, with or without graphical ECG alterations compatible with NSTEACS, without any sign of clinical failure, hypotension, hemodynamic or electric instability will be taken to the “Spoke centre”.

Once the patient has reached the “Spoke centre”, either autonomously or with the territorial emergency system, will undergo an appropriate clinical evaluation (which must imply the attribution of a risk score based on the GRACE protocol), according to which he will follow a process of medical assistance:

- 1) Urgent coronography (within 2 hours) in patients with:
  - Refractory angina
  - Cardiac failure
  - Malignant ventricular arrhythmia
  - Hemodynamic instability
- 2) Early coronography (within 24 hours) in patients with GRACE score >140 or with at least primary criteria of risk:
  - Significant elevation or decrease of troponin
  - Dynamic modifications of ST segment or T wave
- 3) Coronography (within 72 hours) in patients with GRACE risk score 190-140 or with at least one of the following criteria of high risk:
  - Mellitus diabetes
  - Renal insufficiency (GFR <60 ml/min)
  - Left ventricular dysfunction (EF <40%)
  - Early post-infarction angina
  - Recent PCI
  - Previous Coronary Artery Bypass Grafting (CABG)
  - Patients with reoccurring symptoms
- 4) Patients with a low risk (GRACE ≤ 108) in the absence of reoccurring symptoms, the detection of non-invasive inducible ischemia must be performed before deciding for an invasive evaluation.



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