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ORIGINAL ARTICLE

A pilot study on the application of the current European guidelines for the management of acute coronary syndrome without elevation of ST segment (NSTEMI) in the Emergency Department setting in the Italian region Lazio

Studio pilota sull'aderenza alle linee guida europee sulla gestione della sindrome coronarica acuta senza elevazione del tratto ST (NSTEMI) nei Dipartimenti di Emergenza del Lazio

Gabriele Valli[1*], Francesca De Marco[2*], Maria Teresa Spina[3], Valentina Valeriano[4], Antonello Rosa[3], Valentina Minerva[5], Enrico Mirante[5], Maria Pia Ruggieri[2] and Francesco Rocco Pugliese[4], on behalf of Italian Society of Emergency-Urgency Medicine (SIMEU), section of Lazio

ABSTRACT: ***A pilot study on the application of the current European guidelines for the management of acute coronary syndrome without elevation of ST segment (NSTEMI) in the Emergency Department setting in the Italian region Lazio. G. Valli, F. De Marco, M.T. Spina, V. Valeriano, A. Rosa, V. Minerva, E. Mirante, M.P. Ruggieri and F.R. Pugliese, on behalf of Italian Society of Emergency-Urgency Medicine (SIMEU), section of Lazio.***

Background: In 2011 the European Society of Cardiology published the new guidelines for the treatment and management of acute coronary syndrome without elevation of the ST segment (NSTEMI). For the treatment of the syndrome, the use of P_2Y_{12} inhibitors in addition to aspirin was strongly recommended (evidence IA). We studied the application of this recommendation in the setting of the emergency department in the vast and uneven area of the Italian region Lazio, three years after the release of these drugs in Italy.

Methods: 121 consecutive patients (65% older than 65 years) affected by NSTEMI were recruited between May and July 2013. During the transition in the emergency department data was collected on patient's symptoms, syndrome severity and type & timing of treatments chosen. Adherence to the guidelines was evaluated considering the number of "good treated" patients: these being the patients that received at least 80% of the main five recommendations on percutaneous coronary intervention (PCI) timing, antiplatelet and anti-coagulant therapy suggested by the European Cardiology Task Force (ESC guidelines, 2011) for the very acute phase of NSTEMI.

Results: Patients were treated with: 1) 35% of cases with double antiplatelet therapy and anticoagulation (DAPT+AC), 2) 22% of cases with single antiplatelet and anticoagulation (SAPT+AC), 3) 6% of cases with a single antiplatelet therapy (SAPT), 4) 6% of cases with a double antiplatelet therapy (DAPT) and 5) 24% of cases did not receive any therapy. Data on PCI was available for 95 patients and, of these, only 82% of the patients underwent the procedure. The percentage of "good treated" patients were among of 20-40%, depending on PCI timing – as guidelines suggested – was considered as mandatory (20,5%) or as the extreme time limit (40%). Significant differences were found between patients treated in a central hospital with a hemodynamic laboratory active 24/24hr (HUB) and patients treated in the other hospital (SPOKE). HUBs showed a higher percent of "good treated" patients, a higher percentage of early invasive treated and a better adherence to recommended pharmacological therapy.

Conclusions: A significant number of patients did not receive adequate treatment during the emergency department stay. The absence of hemodynamic services increases the risk of inadequate treatment.

Keywords: acute coronary syndrome, antiplatelet therapy, emergency, ischemic heart disease, P_2Y_{12} inhibitors, ASA.

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[1] Department of Emergency Medicine, Giovanni Battista Grassi Hospital, Ostia, Rome, Italy.
[2] Department of Emergency Medicine, San Giovanni Addolorata Hospital, Rome, Italy.
[3] Department of Emergency Medicine, Umberto I Hospital, Sapienza University of Rome, Italy.
[4] Department of Emergency Medicine, Sandro Pertini Hospital, Rome, Italy.
[5] Department of Emergency Medicine, Dono Svizzero Hospital, Formia, Latina, Italy.

** Dr. Valli and Dr. De Marco contributed equally to this article.*

Corresponding author: Gabriele Valli; Via Andrea Doria, 36; I-00192 Roma, Italy; Tel. +39 (0)6 64526050; Fax +39 (0)6 64526050; E-mail address: gabvalli@yahoo.it

Introduction

Coronary disease is the principal cause of death in industrialized countries [1] and Acute Coronary Syndrome (ACS) is the most frequent presentation, contributing greatly to cardiovascular morbidity and mortality. In Italy cardiovascular mortality account for approximately 12% of all the causes of death and among these, ACS account for 8% [2]. ACS syndromes range from unstable angina (UA), myocardial infarction without ST elevation (NSTEMI) to ST elevated myocardial infarction (STEMI); all these syndromes have similar pathophysiology but different symptoms, signs and prognosis, depending on the myocardial damage induced by the arterial hypo-perfusion. Treatment of ACS includes percutaneous coronary intervention (PCI) and antithrombotic treatment. Timing of treatment is critical for patient life expectancy and quality of life. ESC guidelines recommend early PCI and a dual antiplatelet therapy, unless there is a severe risk of bleeding [3]. On the contrary to STEMI in which the treatment is focused on PCI as soon as possible, for NSTEMI the choice of the therapeutic approach is more complex and it is based on careful risk stratification that need specific expertise by the doctors who have the patient in care [4, 5]. In addition, the diagnosis of NSTEMI takes time during which patients remain under the care of the staff of the emergency department (ED). Finally, although patients with NSTEMI are typically admitted promptly after diagnosis, under conditions of hospital crowding, these patients may have prolonged ED stays as they await to be transferred to an inpatient unit or to the catheterization laboratory [6]. For these reasons, it is essential that the emergency physician knows the correct treatment protocols and its applications because it has been demonstrated that when treating patients with ACS, adherence to guidelines is associated with a better patient prognosis [7, 8].

We designed and conducted this study to determine whether differences in NSTEMI patient management exist among the emergency departments of the Italian region Lazio. In particular to estimate differences in the antiplatelet regimen used and to investigate the possible reasons for less than optimal management of these patients. The final purpose is to improve patient care in this region.

Methods

Participation in the study was offered to all institutions and all hospitals of the Italian region Lazio, including university teaching hospitals, general and regional hospitals and private hospitals (7 HUB hospitals with hemodinamic laboratory active 24hr/24hr and 6 SPOKE hospitals without haemodinamic laboratory active 24hr/24hr). Data was collected from seven emergency departments and departments of emergency medicine (5 HUB and 2 SPOKE). Physicians were instructed that participation in the study should not affect clinical care or management. All consecutive patients with NSTEMI, who visited the emergency departments that joined the study from May 2014 to July 2014 were included. Inclusion criteria were: 1. Patients with chest pain and / or symptoms of acute heart failure with at least a determination of troponin positive and who are subsequently transferred or admitted; 2. Age greater than 18 years old; 3. Patients with acute ACS: NSTEMI and UA candidates for urgent invasive strategy (cardiac catheterization followed by revascularization within 120 minutes of arrival in the ED). Exclusion criteria were age <18 years, diagnosis of STEMI and all other causes of chest pain rather than NSTEMI. All patients provided written informed consent, and the study was approved by the ethics committee at each center (protocol number: CE/77926).

Data collection

Data was collected on baseline characteristics including demographics, risk factors and medical history including previous medical therapy (Table 1). Data related to the management in the ED from triage (as color code, if the patient arrived alone or by ambulance, main symptom and ECG) vital sign and relating score (CHEST PAIN score, TIMI risk score, GRACE and CRUSADE score) was collected [3]. Laboratory tests, blood gas analysis, evaluation of ECG and troponin-time 0-6 hours-12 hours, chest X-ray and other diagnostic tests (chest CT scan without and with contrast medium for possible differential diagnosis: pulmonary embolism, aortic disorder), cardiac ultrasound were also recorded. Finally, we collected data related to medical therapy administered and invasive procedure performed – coronary angiography, urgent/elective – outcome (discharge/transfer/death) and diagnosis (see Table 2, 3 and Figure 2).

Guidelines Adherence Evaluation

The main objective of the study was to evaluate agreement between the ED management of NSTEMI patients in our local regional hospitals with the ESC recommendation published in 2011 (ESC, 2011). Adherence scores were calculated by assigning one point for prescription of any of each of the following treatments as recommended for acute therapy in ESC guidelines: early aspirin (ASA) administration, P_2Y_{12} inhibition, early anticoagulation, gastric protection with proton pump inhibitors (PPI) for high bleeding risk patients. One point more was added in cases where the PCI was performed with correct timing, according to the risk stratification of the patient and the ESC guidelines. The PCI timing adherence was considered in the two following possible approaches: the more conservatory one that considered the time range suggested by the guidelines as mandatory (PCI_{ontime}), and the early revascularization approach which considered the time range recommended as the maximal time limit for the PCI ($PCI_{within\ time}$). One point was assigned when a treatment was not prescribed because of major contraindication to treatment or because treatment was unnecessary (i.e. PPI in patients at low risk of bleeding) because this was considered to be adherence, and thus reducing bias in the interpretation of guidelines adherence. The score for each patient was expressed as a percentage of the maximum possible score (five points) and "Good treated patients" were defined as an adherence score greater than or equal to 80% (at least four of the recommended treatments).

Table 1. - Percent of patients resulted positive to one of the main risk factors, co-morbidity or indexes of severity. Data are shown both as total (TOT) and grouped according to risk stratification proposed by ESC guidelines 2011 (Low, Intermediate, High, Very High). χ^2 tests the null hypothesis that there are no differences among the risk groups' distributions of the analyzing variables

RISK STRATIFICATION ACCORDING WITH E.S.C. GUIDELINES 2011						
	TOT *(% tot)*	LOW *(% row)*	INTERMEDIATE *(% row)*	HIGH *(% row)*	VERY HIGH *(% row)*	*P*
Age > 65yrs	**79 (65%)**	2 (2%)	43 (54%)	31 (39%)	3 (4%)	*0.01*
Male	**71 (59%)**	4 (6%)	47 (66%)	18 (25%)	2 (3%)	*NS*
Familiarity	**15 (12%)**	3(20%)	11 (73%)	1 (7%)	-	*0.01*
Smoking	**25 (20%)**	2 (8%)	19 (76%)	3 (12%)	1 (4%)	*NS*
No Risk Factors	**10 (8%)**	-	7 (70%)	3 (30%)	-	*NS*
Hypertension	**93 (77%)**	3 (3%)	56 (60%)	32 (34%)	2 (2%)	*NS*
Diabetes	**31 (26%)**	-	15 (48%)	16 (51%)	-	*0.05*
Cardiovascular Diseases	**38 (31%)**	-	21 (55%)	16 (42%)	1 (2%)	*NS*
Renal Failure	**10 (8%)**	-	7 (70%)	3 (30%)	-	*0.01*
Other diseases	**50 (41%)**	2 (4%)	34 (68%)	12 (24%)	2 (4%)	*NS*
Red Code	**43 (35%)**	1 (2%)	18 (41%)	21 (49%)	3 (6%)	*0.0001*
CPS>4	**79 (65%)**	3 (4%)	52 (65%)	23 (29%)	1 (1%)	*NS*
TOT (%of tot)		**5 (4%)**	**76 (63%)**	**37 (31%)**	**3 (2%)**	**--**

Table 2. - Timing of PCI grouped by risk stratification according with E.S.C. Guidelines 2011. Patients that exactly match PCI timing suggests by guidelines are grouped in the black cells, in the light grey cells patients treated earlier than the time suggested, while patients that were treated later than recommended are grouped in the dark grey cells

RISK STRATIFICATION ACCORDING WITH E.S.C. GUIDELINES 2011

Timing of PCI	LOW	INTERMEDIATE	HIGH	VERY HIGH	TOT
PCI <120 min	0	10	3	3	16
120min> PCI< 24hr	2	24	7	0	33
24hr>PCI< 72hr	2	9	15	0	26
PCI>72hr	0	4	3	0	7
NEVER	0	6	7	0	13
ToT	4	53	35	3	95

Management of Data Collection on database

Database management and statistical analysis will be carried out in the center of reference of the Head of the study, defined by the Regional Executive Board of *Italian Society of Emergency-Urgency Medicine (SIMEU)*, section of the region Lazio.

Data Analysis and Statistics

Data for all the patients enrolled in the study (the study population) were analyzed. Mean and standard deviation (SD) were calculated for continuous variable and the number and percentage in relation to the total number of patients were calculated for

qualitative variables. Looking for possible difference in treatment strategy, we grouped data in four different risk classes (low risk, intermediate risk, high risk and very high risk) according with the risk stratification suggested by ESC guidelines [3] and data within the groups were compared. In order to better understand significant difference in patient management depending on hospital skills, we stratified patients according to the hospital of enrollment dividing the sample in two additional groups: patients enrolled in hospital without a hemodynamic laboratory active 24hr/24hr (SPOKE) and patients enrolled in hospital with hemodynamic laboratory active 24hr/24hr (HUB). Variables were tested for independency and homogeneity in the distribution of the different groups by Fisher's exact test. Observed differences are expressed as p values. A value of $p<0.05$ was considered statistically significant. All analyses were performed with SPSS system software (*IBM SPSS statistics*, Version 20.0, *SPSS Inc*., Chicago). Completeness of data was 100% for all the analyzed variables, with the exception of variables describing the data about PCI that were completed only for 95 patients (79%).

Results

Patients studied

Data came from 7 different EDs among the 13 that initially endorsed the study: 83% of the patients enrolled from public non-university hospital, 12% from public university hospitals, 6% from a private hospital. A hemodynamic laboratory was active 24hr/24hr in 5 of the 7 hospitals involved (60% of all the cases enrolled). The number of patients enrolled into the study was 139; of these 121 patients (87%) were eligible for analysis. Of the 18 patients (13%) not eligible for analysis, the reasons for exclusion were a troponin increase not related to a coronary syndrome (15 patients) and data unusable or incomplete (3 patients). The final diagnosis of these 15 patients with a non-specific increase in troponin was: acute pulmonary edema (6 patients), septic shock (3 patients), pneumonia (3 patients), myocarditis (1 patient), severe anemia (1 patient), and respiratory failure (1 patient).

Demographic characteristics, risk factors and co-morbidities of the patients were summarized in Table 1. Patients who were older than 65 years old were 65% of the cases, with a risk significantly higher than the younger ones (p 0.01). Only 15 patients had familiarity for cardiovascular diseases; 20% of the patients were smokers but smoking habit was not correlated with a more instable condition at the presentation. In 10 cases, patients had no known risk factors. At least one concomitant disease was present in 94% of the cases with an average of 2.3±1.5SD concomitant co-morbidities. The most frequent disease was hypertension (77% of the patients) but diabetes and renal failure were associated with a higher risk rank at presentation.

In 35% of the cases, it was assigned the greatest urgency code at the entrance, the red code, in 20% of the cases in patients that were at intermediate risk. Chest Pain Score (CPS) was higher than 4 in 65% of the cases.

Treatment of choice in ED

Figure 1 summarized the therapy administrated to the patients during the stay in ED (panel a) and the drugs that were more frequently utilized (panel b).35% of the patients received the recommended triple therapy with double antiplatelet treatment and anticoagulation (DATP+AC), 41% patients received an incomplete antithrombotic therapy and 24% of the patients (29 patients) did not receive any therapy during the transition in emergency room. In this last group of untreated patients, 48% was not in a chronic antiplatelet therapy, 48% had a CRUSADE score less than 41 (low hemorrhagic risk) and in only 4 cases the PCI was performed in less than 120 min, which could justify the absence of treatment in ED because of urgent transfer to the hemodynamic laboratory; 48% of patients treated in a SPOKE hospital did not receive any therapy versus 15% of HUB ($p<0.001$).

The most frequent antiplatelet drug used was ASA (Figure 1b), administrated to 59% of all treated patients, followed by ticagrelor and clopidogrel. Prasugruel was never used, even though strongly indicated in diabetic patients, possibly because of the very rare occurrence of a known coronary anatomy at the moment of the ischemic event [3, 9]. ASA was

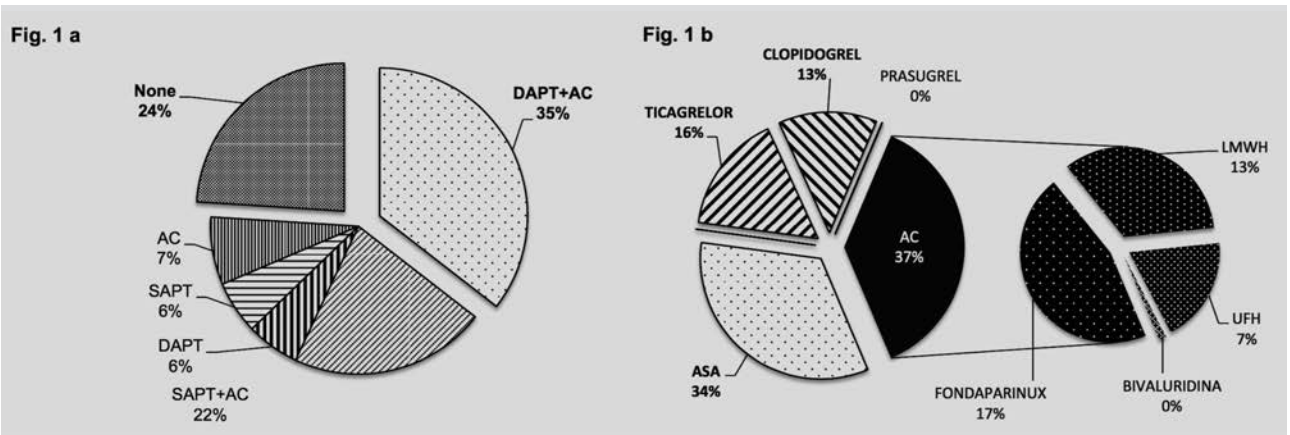

Figure 1. - Therapeutic scheme chosen (panel A) and drug utilized (panel B) during the patient's stay in the emergency room. DAPT+AC, double antiplatelet therapy and anticoagulation; SAPT+AC, single antiplatelet therapy and anticoagulation; DAPT, double antiplatelet therapy without concomitant anticoagulation; SAPT, single antiplatelet therapy without anticoagulation; AC, single anticoagulation without any anti platelet therapy.

administrated in 98-100% of patients treated with antithrombotic strategy who underwent a double antiplatelet therapy (Figure 2a) or when the antiplatelet was the only drug administrated. When the strategy was a single antiplatelet drug together with the anticoagulation, the antiplatelet agent used was in 60% of cases ASA, in 27% ticagrelor and in 15% of cases clopidogrel.

The most frequent anticoagulant used was fondaparinux (30% of all cases), followed by low molecular weight heparin (LMWH: 22% of all cases) and unfractioned heparin (UH: 12% of all cases); bivalirudin was used in only two cases. Fondaparinux was preferred when a DAPT+AC was chosen (56%, Figure 2b), while LMWH was most frequently used when the only therapy administrated was the anticoagulation (67%, Figure 2b).

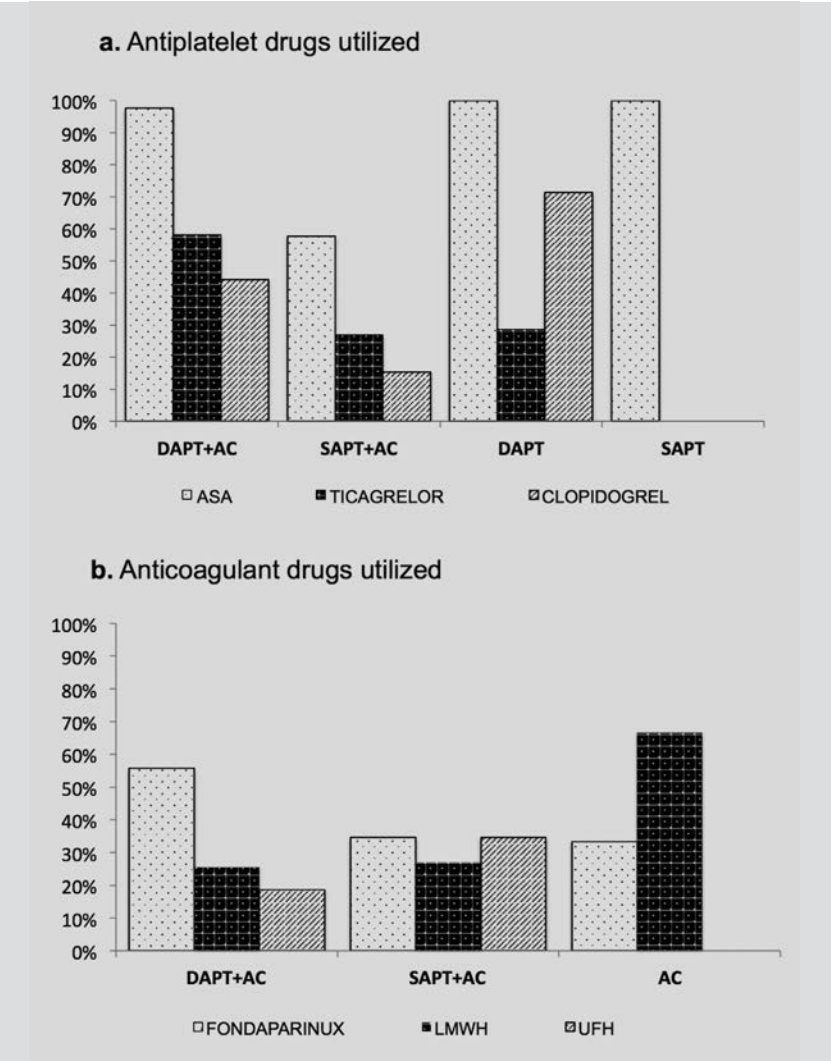

Figure 2. - Percent of drugs utilized during the emergency stay of the patient, grouped by therapeutic scheme. Panel a summarized the antiplatelet therapy while data on anticoagulant therapy are represented in panel b. DAPT+AC, double antiplatelet therapy and anticoagulation; SAPT+AC, single antiplatelet therapy and anticoagulation; DAPT, double antiplatelet therapy without concomitant anticoagulation; SAPT, single antiplatelet therapy without anticoagulation; AC, single anticoagulation without any anti platelet therapy. ASA, aspirin; LMWH, low molecular weight heparin; UFH, unfractionated heparin.

Timing of PCI

Data on PCI are available for 95 patients (79% of the sample); of the 82 patients who underwent a PCI: 16 patients underwent the procedure within 120 min from the hospital admission, 33 were still treated within 24hrs, 26 in the period between 24 and 72hrs and 7 patients more the 72hrs later. In Table 2 data categorized among the PCI timing with respect to the risk of death, according to ESC guidelines, are shown [3]. As shown in the Table, only 20% of the patients treated strictly followed the guidelines, 43% of the patients underwent PCI earlier than suggested while 37% achieved PCI later than recommended. A significant difference in timing of PCI was observed between SPOKEs and HUBs. As shown in Figure 3 only a small percentage of cases completely matched the ESC guidelines but, while in HUB centers the great majority of the cases were treated earlier than the recommended time (70% of the cases treated in a HUB hospital), a significant percent of cases were treated too late the PCI in the SPOKE centers (58% of the cases treated in a SPOKE hospital).

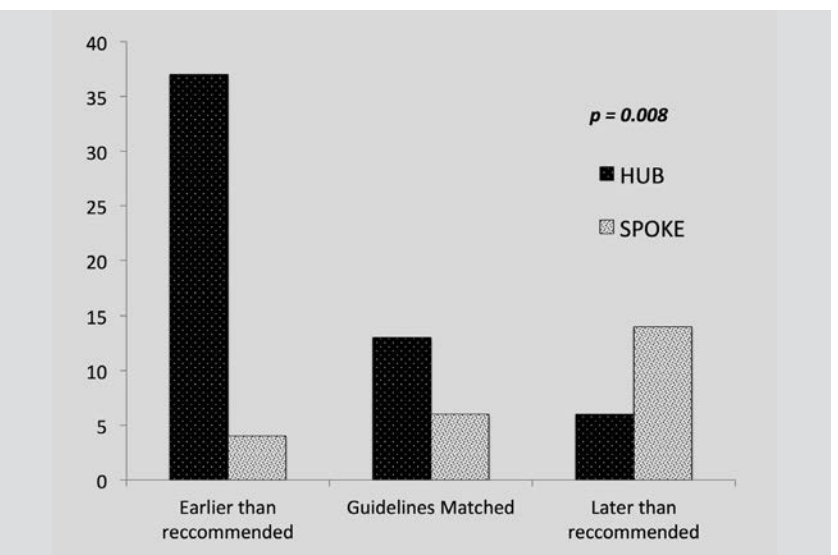

Figure 3. - Percent of patients, treated in a HUB (light columns) or in a SPOKE (dark columns) hospital, which matched the guidelines recommendation on timing of PCI, which were treated earlier than recommended or which were treated later than recommended. Patients treated in a SPOKE performed the PCI significantly later than patients treated in a HUB ($p<0.001$).

Adherence to Guidelines

Analyzing the global adherence to guidelines in the setting of the ED, in accordance with the system described previously, the proportion of patients in the evaluable patient population with a "good" adherence

score (adherence score greater than or equal to 80%) at discharge was 26.3% considering the PCI timing recommended by ESC guidelines as mandatory and 40.0% if it considered as a maximum time limit. Stratifying for the cardiovascular risk did not add any relevant information.

As shown in Figure 4, no significant differences were found between HUB and SPOKE in terms of adherence to guidelines recommended for PCI timing when it was considered PCI performed exactly at the time recommended by ESC guidelines (HUB vs SPOKE, 18.3% vs25.0%, p=0.557), while, considering PCI performed within the time recommended, the proportion of patients with a good adherence score was significantly higher in HUB with respect to SPOKE (HUB vs SPOKE, 83.1% vs62.5%, p<0.05).

Adherence to 80% of the pharmacological therapy recommendations was of 42.1%; no significant difference between HUB and SPOKE was found (respectively HUB vs SPOKE, 38.8% vs51.4%, p=0.23). Individually analyzing the four relevant ESC guidelines recommendation on urgent NSTEMI therapy (ASA administration as soon as possible, P_2Y_{12} inhibition, urgent anticoagulation and gastric protection in high bleeding risk subjects) we found that the rate of adherence was respectively: 58.7% for ASA administration, 48.8% for P_2Y_{12} inhibition, 64.5% for urgent anticoagulation and 34.7% for gastric protection in high risk subjects.

Significant differences between HUB and SPOKE (Figure 4) were found in ASA administration (respectively 69.8% vs 31.4%, p<0.0001), P_2Y_{12} inhibition (respectively 54.7% vs 34.3%, p<0.05) and urgent anticoagulation (respectively 69.8% vs 51.4%, p<0.05). No other relevant differences were found.

Discussion

The main findings of the study were a percentage of surprisingly low "good treated patients" and a significant inhomogeneity among the different setting of the region Lazio, with a significant difference between HUB versus SPOKE.

To our knowledge, this is the first study that analyzed the ACS guidelines adherence in the particular setting of the ED. Italian registry on NSTEMI data were usually collected from cardiology department rather than first aids and ED [5, 10-12]; however, ED remains a crucial setting for the diagnosis and first treatment of these patients. NSTEMI patients usually remain for a quite long period under the care of ED caregiver before the admission to a more specialized or intensive care ward. The long stay in ED of these patients was associated with a decreased use of guideline-recommended therapies [6]. Data from our study are not perfectly overlapped with the previous Italian surveys, not only for the different setting where data was collected (ED versus specialist ward), but also because surveys referred to a previous version of European guidelines recommendation in which the indications to the use of the new P_2Y_{12} inhibitors drugs (i.e. ticagrelor, prasugrel) was not so strong yet. We found that the overall percentage of ASA use was

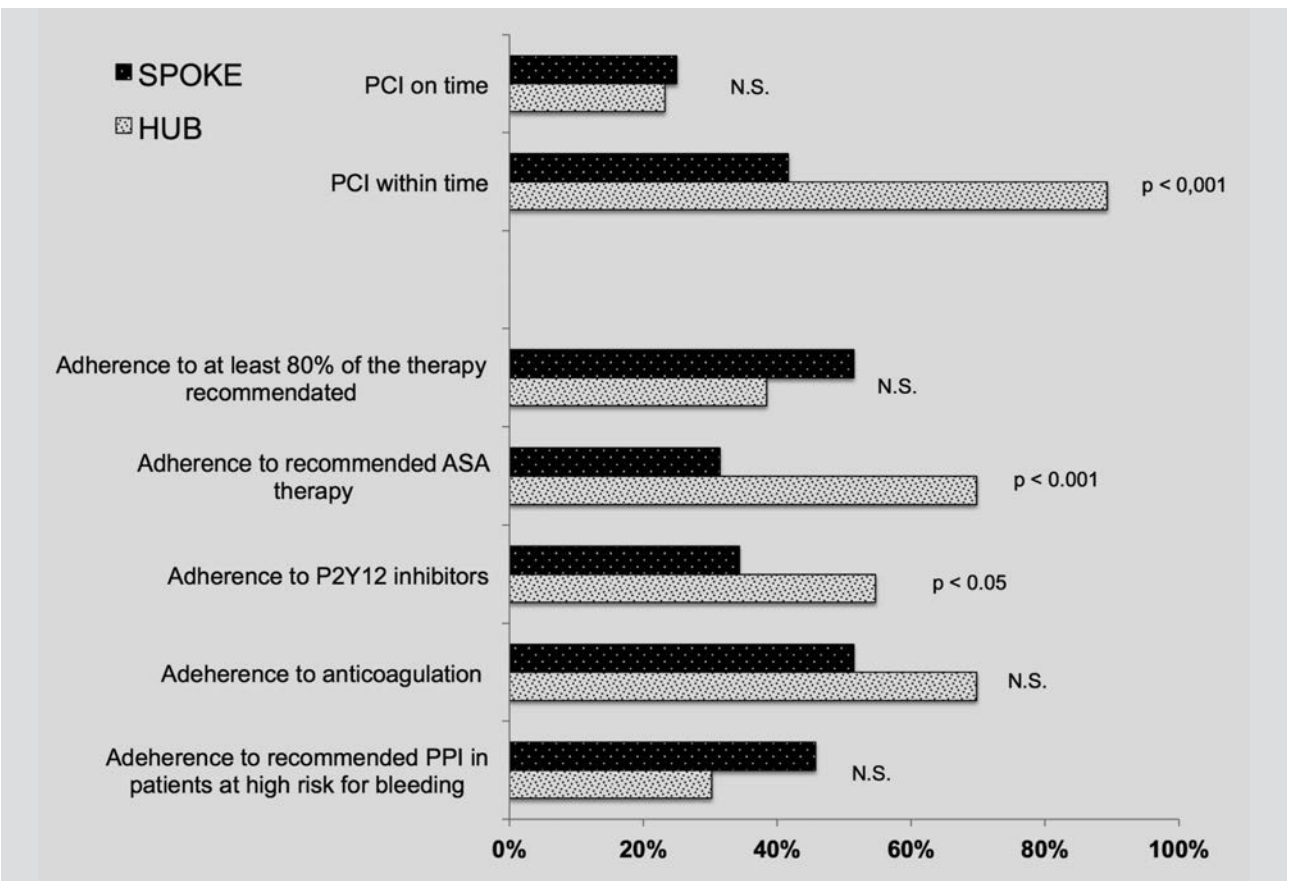

Figure 4. - Percent of adherences to guidelines recommendations on PCI timing and antithrombotic therapy, among the SPOKE hospitals (dark columns) and the HUB hospitals (light columns).

only 59%, a percentage slightly lower than what was observed in other previous studies: 95% in the R.Os.A.I. -2 [5], 87% in BLITZ-1 [10], 95% in BLITZ-2 [11] and 75% in BLITZ-4 [12]. Also when comparing our findings to International surveys, the use of antiplatelet therapy is lower. In the two *Euro Heart Surveys* on ACS (ACS-I, ACS-II), for example, the percentages of ASA and P_2Y_{12} antagonist administration were 88.5% and 94.5% for ASA and 27.6% and 67.4% for thienopyridine respectively in ACS-I [13] and ACS-II [14]. The percentage of patients treated with ASA rose up till 98% if we considered the population of patient treated with any kind of platelet inhibitory therapy; this difference could depend on the different settings of the study: patients that did not receive any therapy in the ED were likely to be admitted to a non-specialist ward (i.e. internal medicine ward) and did not appear in a registry that considered only patients admitted in a cardiology setting. ASA was the drug more frequently administrated during the ED stay, all the other medications were given in less than 30% of the patients regardless of the kind of therapy (antiplatelet or anticoagulant). Percentages of patients that did not receive any therapy (i.e. 24%) and who did not receive an optimal therapy (41%) were quite high. Also analyzing guidelines adherence to the recommended pharmacological therapy, both if it has been evaluated as a whole or if it has been assessed for each specific recommendation, the percentage of application was about 40%. On the other hand, PCI was preformed in 86% of the cases, independently from the features of the hospital that enrolled the case. Compared to previous Italian surveys, this percentage of treatment is significantly higher: in the AI-CARE2 study, for example, only 43% of the patients without a ST segment elevation, underwent an invasive procedure [15]. The disproportion between pharmacological therapy adherence and PCI treatment is an extremely interesting difference. It indicates that PCI is considered a mandatory treatment for ACS while the emergency physician did not perceive antiplatelet and anti-coagulant therapy as urgent. In fact, the usefulness of an early invasive strategy in NSTEMI is still on debate [16, 17] and ESC guideline, still in 2014, recommended to reserve the invasive strategy to intermediate risk patients and the early invasive treatment strategy only in high risk patients [18]; on the other hand the same guidelines strongly recommended to start the double antiplatelet therapy and the anti-coagulation therapy as soon as possible.

The observed differences between HUB and SPOKE hospitals in guidelines adherence is not so surprising. The same finding was already observed in Italian registry, as in the BLITZ-2 study [10], or in international studies [19]. According to the present investigation, in everyday clinical practice patient selection for coronary-angiography timing does not seem to depend on the risk stratification. The HUBs hospital seem to over-treat patients with NSTEMI directing patients to perform the procedures very early (Figure 3), while SPOKE centers delay the procedure behind the 72hr limit, even with patients at high risk. One possible explanation is the ready availability of the procedure that could justify the early transfer of the patient in catheterization laboratory. The problem is that, in a system in which HUB structures have the responsibility to absorb and treat patient coming from SPOKE centers, the secondary effect of HUB's over treatment patients who can delay the procedure is not only waste of resources without reducing the risk of death among the population afferent to that hospital [20], but it is also to reduce receptiveness from SPOKE structures. As a consequence, the treatment of patients who refer to these peripheral structures was delayed with a potentially increase risk of death for these sub-population [21].

The ease of access to the procedure, however, is not the only explanation of the differences. The same differences were observed also in pharmacological approach. HUB patients received the correct pharmacological therapy more frequently than SPOKE (Figure 4). The reasons for these differences are unclear. The first possible explanation is the presence of highly skilled and updated staff that guarantee a better adherence to the last guidelines in HUB center, because of the presence of the catheterization laboratory. The other possible explanation, more speculative but that we should consider, is that SPOKE hospitals are usually smaller and with less hospitalization capacity; patients are used to wait longer for the correct place and the prolonged ED stays are shown to be correlated with a worse adherence to the guidelines [22]. Regardless of what is the cause, better organization of the network would be desirable.

Limitations of the study

There are several issues that should be considered in the interpretation of the results of this study. First, the sample is very small and the ratio between the data from structures SPOKE is disproportionately small compared with the data from the structures HUB and this may have influenced the results. Few SPOKE structures were involved and a certain amount of data regardless PCI for patients treated by SPOKE structures was lost. This reflects the difficulty retrieving data when the patient has been transferred from a peripheral structure to other hospitals. Furthermore highlights the limited cooperation of the network in the daily reality. Current privacy regulations that restrict anonymous data collection after hospital transfer also limit the data collection.

Secondly we did not analyze data regarding time spent in the ED before hospital admission or number of patients transferred to another hospital to complete the diagnosis and treatment procedures.

Thirdly we have no data on clinical outcome of the patients that could be really significant to understand how much the differences observed had a real impact on clinical outcome of the patients.

Last, it is not possible to adjust for or identify intentional omissions of patients or differences in skill of the doctors whose care did not meet quality standards; thus, the discrepancies, if present, are expected to be uniform across all sites.

Conclusion

This is the first pilot study that analyzed treatment of ACS - NSTEMI, in the specific setting of ED in the

Italian region Lazio. The real life adherence to the European Society of Cardiology recommendations were significantly lower than expected with a great discrepancy between HUB and SPOKE hospitals. Patients referred to SPOKE Hospitals did not match the guidelines as frequently as the others. A closer collaboration in the ACS network would be desirable to improve guidelines adherence in the entire region, in order to guarantee a better level of assistance to all patients regardless in which hospital the patient was treated.

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