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# Contemporary Antithrombotic Strategies in Patients with Acute Coronary Syndromes Managed without Revascularization: Insights from the EYESHOT Study

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**ABSTRACT**

**Background**. Patients with acute coronary syndromes (ACS) who are managed without coronary revascularization represent a mixed and understudied population that seems to receive sub-optimal pharmacological treatment.

**Methods.** We assessed patterns of antithrombotic therapies employed during the hospitalization and in-hospital clinical events of medically managed patients with ACS enrolled in the prospective, multicenter, nationwide EYESHOT registry.

**Results.** Among the 2585 consecutive ACS patients enrolled in EYESHOT, 783 (30.3%) did not receive any revascularization during hospital admission. Of these, 478 (61.0%) underwent coronary angiography while 305 (39.0%) did not. The median GRACE and CRUSADE risk scores were significantly higher among patients who did not undergo coronary angiography compared to patients who did (180 vs 145, $p<0.0001$, and 50 vs 33, $p<0.0001$, respectively). Antithrombotic therapies employed during hospitalization significantly differ between patients who received coronary angiography compared to those who did not, with unfractioned heparin and novel P2Y12 inhibitors more frequently used in the first group, and low-molecular weight heparins and clopidogrel in the latter group. During the index hospitalization, patients who did not receive coronary angiography presented a higher incidence of ischemic cerebrovascular events and of mortality compared to patients who underwent coronary angiography (1.6% vs 0.2%, $p=0.04$ and 7.9% vs 2.7%, $p=0.0009$, respectively).

**Conclusion**. Almost one-third of ACS patients are managed without revascularization during the index hospitalization. In this population, a lower use of recommended antiplatelet therapy and worse clinical outcome was observed in those who did not undergo coronary angiography as compared with those who did.

**Key words:** acute coronary syndromes; conservative strategy; antithrombotic therapy; prasugrel; ticagrelor; anticogulants.

## INTRODUCTION

Patients with acute coronary syndromes (ACS) who are managed without coronary revascularization represent a heterogeneous and understudied population (1). This subgroup of patients appears to receive sub-optimal pharmacological treatment, with an under-use of guideline-recommended antithrombotic drugs at the time of hospital discharge, which may contribute to worse prognosis (2-5).

Among medically managed patients, two distinct groups can be identified: patients who are not submitted to coronary angiography (CA) and those who are not revascularized after CA. While the latter population presents a low mortality rate at short-term that remains stable over time, the first group appears to show a progressive increase in mortality over the years (2-5).

Using data from the EYESHOT (EmploYEd antithrombotic therapies in patients with acute coronary Syndromes HOspitalized in iTalian cardiac care units) registry, we sought to examine patterns of antithrombotic therapies prescribed during the index hospitalization among medically managed patients with ACS.

## METHODS

EYESHOT was a multicentre, observational, prospective, nationwide study aimed to evaluate in-hospital use of antithrombotic therapies in consecutive ACS patients admitted to the Italian intensive cardiac care units (CCUs) during a period of 3 weeks. Inclusion criteria have been detailed elsewhere (6). Briefly, patients ≥18 years old admitted to a CCU with a diagnosis of ACS were eligible if they had cardiac ischemia-related symptoms of ≥10 minutes duration and (a) concurrent biomarker evidence of ACS and/or (b) concurrent electrocardiographic changes.

The Italian National Association of Hospital Cardiologist (ANMCO) designed the study and invited to participate all Italian hospitals, including university teaching hospitals, general and regional hospitals, and private clinics with CCUs receiving ACS patients (6).

Informed consent was obtained from all patients, who were informed of the nature and aims of the study. Local Institutional Review Boards were informed of the study according to the Italian rules. The study was registered on ClinicalTrials.gov (ID: NCT02015624).

**Data collection and data quality**

Data on baseline characteristics, including demographics, risk factors and medical history, were collected. Information on the use of cardiac procedures, including CA and its timing, use of medications, and in-hospital major clinical events, were recorded.

An emphasis was given to the collection of data regarding antithrombotic therapies administered and within class changes of antithrombotic drugs [eg different $P2Y_{12}$ inhibitors (switching)] during hospitalization and at discharge].

Myocardial infarction/re-infarction during index hospitalization was diagnosed in the presence of new ischemic symptoms and an elevation (or re-elevation) of biomarkers of myocardial necrosis with or without concurrent ECG changes. Major bleeding was classified according to the Thrombolysis In Myocardial Infarction (TIMI) criteria (7). Stroke was identified as an acute neurologic deficit that lasted >24 hours and affected the ability to perform daily activities with or without confirmation by imaging techniques.

At each site, the principal investigator was responsible for screening consecutive patients admitted to the CCU. Data were collected using a web-based, electronic CRF with the central database located at the ANMCO Research Center. By using a validation plan, integrated in the data entry software, data were checked for missing or contradictory entries and values out of the normal range.

**Statistical analysis**

Categorical variables are presented as number and percentages and compared by the chi-squared test. Continuous variables are presented as mean and standard deviation (SD) with the exception of

GRACE (Global Registry of Acute Coronary Events) (8) and CRUSADE (Can Rapid Risk Stratification of Unstable Angina Patients Suppress Adverse Outcomes with Early Implementation of the ACC/AHA Guidelines) (9) risk scores, time to CA, and length of hospital stay, which are reported as median and inter-quartile range (IQR). Continuous variables were compared by the *t* test, if normally distributed, or by the Mann-Whitney U test, if not.

In the present analysis we divided the population of interest (ie medically managed patients with ACS) into two groups: (1) patients not undergoing CA (no CA group); (2) patients not revascularized after CA (after CA group).

All the variables which were statistically significant at univariate analysis (see figure legends for details) were included in a multivariable model (logistic regression), to identify the independent predictors of: a) not receiving CA in the entire EYESHOT population, b) not receiving revascularization among patients who underwent CA, excluding patients without significant coronary stenoses, and c) lack of prescription at discharge of dual antiplatelet therapy (DAPT), defined as aspirin plus a P2Y12 inhibitor, in medically managed patients. The variables included in the latter logistic mode were: geographic area of the hospital, hospital without Cathlab, history of anemia/major bleedings, bleeding during hospitalization, extent of CAD, indication to CABG. Gender and age were forced into the model, even though not statistically significant at the univariate analysis. When more than two categories were present, dummy variables were introduced to define a reference group.

A p value $< 0.05$ was considered statistically significant. All tests were 2-sided. Analyses were performed with SAS system software, version 9.2.

**RESULTS**

During the 3-week study periods (from December 2 to December 22, 2013 and from January 27 to February 16, 2014), a total of 2585 consecutive patients have been enrolled in 203 CCUs across

Italy. The proportion of patients managed without revascularization differed between NSTEACS and STEMI. Of the 1519 patients with an initial diagnosis of non ST-elevation (NSTE)-ACS, 649 (42.7%) were managed medically. Of these 388 (59.8%) underwent CA while 261 (40.2%) did not. Among the 1066 ST-elevation myocardial infarction (STEMI) patients, 134 (12.6%) were managed medically. Of these, 90 (67.2%) underwent CA while 44 (32.8%) did not. Therefore, a total of 783 (30.3%) patients with ACS were managed without revascularization: 478 (61.0%) underwent CA and 305 (39.0%) did not (Figure 1).

Baseline clinical characteristics and variables are summarized in Tables 1 and 2. Patients in the 'no CA' group presented a significantly higher incidence of cardiovascular risk factors including hypertension, renal dysfunction, malignancy, and a history of cardiovascular diseases compared to patients in the 'after CA' group. This is reflected by an higher median GRACE and CRUSADE risk scores among patients who did not undergo CA as compared to patients who did.

Multivariable analysis yielded several independent predictors of not receiving CA (Figure 2): the most powerful predictor was the absence of a cath lab on site [Odds Ratio (OR): 12.78; 95% Confidence Interval (CI) 9.13-17.89, $p<0.0001$], followed by malignancy (OR 8.99; 95% CI 4.35-18.59; $p<0.0001$) and age ≥75 years (OR 2.79; 95% CI 1.94-4.02; $p<0.0001$).

**Angiographic and Procedural Data in Patients who Underwent Angiography**

Among patients who underwent angiography (n=478), a radial approach was used in 75.7% and a PCI was unsuccessfully attempted in 7.7% of cases. The absence of significant coronary stenoses at CA was observed in 31.6% of patients, while 1-vessel disease, a 2-vessel disease and a 3-vessel disease were present in 24.2%, 16.3% and 28.0% of cases, respectively.

One-hundred-one (23.2%) patients out of the 478 who underwent CA have been discharged with an indication to coronary artery by-pass (CABG).

The median time from hospital admission to angiography was 33.3 hours [inter-quartile range (IQR)

11.7-69.1] in hospitals with CathLab and 59.8 hours (IQR 38.4-118.5) in those without CathLab ($p<0.0001$). This timing differed among STEMI [2.5 hours (IQR 1.3-29.8) in hospitals with CathLab and 10.6 hours (IQR 2.1-50.9) in those without CathLab, $p=0.33$] and NSTE-ACS patients [40.5 hours (IQR 19.8-73.5) in hospitals with CathLab and 67.2 hours (IQR 42.5-126.7) in those without CathLab, $p<0.0001$].

At multivariable analysis and excluding patients without significant stenoses at angiography, the diagnosis of NSTE-ACS vs STEMI (OR: 3.27; 95% CI: 2.36-4.53, $p<0.0001$), the admission to an hospital without cath lab (OR: 1.80; 95% CI: 1.27-2.55, $p=0.0009$) and the presence of a 3-vessel disease (OR: 1.52; 95% CI: 1.16-2.01, $p=0.003$) resulted as the most powerful predictors of medical management (Figure 3).

**Antithrombotic therapies during hospitalization**

Figure 4 shows antithrombotic therapies administered during hospitalization in patients managed conservatively with or without CA. Overall, aspirin was administered to 90.8% of patients, a $P2Y_{12}$ inhibitor in 81.5%, glycoprotein IIb/IIIa inhibitors in 1.4%, unfractioned heparin (UFH) in 39.6%, low-molecular weight heparins (LMWH) in 48.4%, fondaparinux in 18.7% and bivalirudin in 1.0% of patients.

Among medically managed patients in the ‘no CA’ compared to ‘after CA’ group, low-molecular weight heparins (58.4% vs 42.1%, $p<0.0001$), and clopidogrel (64.9% vs 55.2%, $p=0.007$) were more frequently used, while unfractioned heparin (10.2% vs 58.4%, $p<0.0001$), aspirin (87.2% vs 93.1%, $p=0.006$), ticagrelor (10.8% vs 26.2%, $p<0.0001$) and prasugrel (1.0% vs 3.6%, $p=0.03$) were less commonly employed (Figure 4).

A switching of $P2Y_{12}$ inhibitor occurred in 5.7% of patients: 3.2% of patients in the ‘no CA’ group and 7.3% among patients in the ‘after CA’ group. Overall, an upgrade from clopidogrel to novel $P2Y_{12}$ inhibitors occurred in 2.0%, a downgrade from novel $P2Y_{12}$ inhibitors to clopidogrel or

ticlopidine in 3.2% and a change within novel $P2Y_{12}$ inhibitors (ticagrelor/prasugrel or viceversa) in 0.3%.

Antithrombotic therapies prescribed among medically managed patients discharged alive with a final diagnosis of STEMI and NSTE-ACS are shown in Table 3. At discharge, DAPT was prescribed to 58.8% and aspirin alone in 29.2% of medically managed patients. At multivariable analysis, the predictors of non-prescription of DAPT at discharge were the indication to CABG (OR 9.87; 95% CI 5.39-18.08; p<.0001), the absence of coronary stenoses at angiography (OR 3.41; 95% CI 1.96-5.92; p<.0001), the recurrence of bleeding events during the hospitalization (OR 5.28; 95% CI 2.43-11.47; p= p<.0001), a history of bleeding (OR 1.81; 95% CI 1.09-2.99; p=0.02). On the other hand, an admission to a CCU located in the South of Italy was associated to a lower risk of no DAPT prescription (OR 0.53; 95% CI 0.38-0.74; p=0.0002).

**In-hospital clinical events**

Median hospital stay was 7 days (IQR 5-11) for patients who did not undergo a CA and 6 days (IQR 4-9) for patients who did (p<0.0001). The incidence of in-hospital clinical events among STEMI and NSTE-ACS patients managed without revascularization are shown in Figure 5. Overall, the rate of myocardial (re)infarction in patients in the 'no CA' and 'after CA' groups was 0.7% and 0.2% (p=0.56), major bleeding was 3.0% and 1.5% (p=0.15), stroke/TIA was 1.6% and 0.2% (p=0.04), and mortality was 7.9% and 2.7% (p=0.0009), respectively. The mortality ranged from 2.1% in patients with NSTE-ACS and CA to 18.2% in patients with STEMI and no CA.

**DISCUSSION**

Our study shows that, in a contemporary cohort of consecutive ACS patients: 1) Conservative management is still adopted in a substantial proportion of patients, mainly presenting with NSTE-

ACS; 2) Patterns of antithrombotic therapies used and in-hospital outcome are distinct in those who received CA as compared to those who did not.

The use of a conservative strategy in the contemporary management of ACS may vary considering randomized clinical trials and real world data (2-5, 10-13). A recent trial in all comers NSTE-ACS population showed that approximately one third of patients were managed without revascularization (14). Similarly, recent international registries have shown that approximately 40% of patients hospitalized with a diagnosis of ACS have not received coronary revascularization during hospitalization (2-5). These data are in agreement with our series where approximately 43% of NSTE-ACS and 13% of STEMI patients received a conservative strategy. Notably, the number of medically managed patients observed in our registry might be overestimated since 23% of patients who underwent CA have been discharged with an indication to surgical coronary revascularization. Nevertheless, the number of patients who received a planned or unplanned revascularization after discharge is unknown. Therefore, the number of patients receiving a conservative strategy in this analysis refers only to the index hospitalization for ACS.

Possible reasons for patients not undergoing in-hospital revascularization include death before planned revascularization, serious comorbidities, resource availability, socioeconomic disparities, a long time delay between hospital arrival and coronary angiography due to organizational issues, absence of coronary stenoses, patient refusal or unfavourable coronary anatomy. Unfortunately, in our registry we did not collect data on coronary lesion complexity, therefore we cannot quantify the number of patients judged unsuitable for revascularization by physicians. In our analysis, the strongest independent predictors of medical management (as opposed to a revascularization) was the lack of a cath lab on site. Also malignancy, older age, and dementia were strongly associated with a conservative strategy.

These findings underline the importance to distinguish two different populations among medically managed patients: those who do not even receive CA, mainly because of their high clinical risk due

to severe comorbidities and advanced age, and patients who are not revascularized after CA due to low anatomic risk (subcritical coronary artery disease or obstructive disease of a secondary vessel) or, more rarely, due to the presence of a severe and extensive obstructive coronary artery disease not eligible for revascularization. These two groups have different therapeutic strategies and prognosis (15), as also confirmed in our study, where patients not undergoing CA compared to patients not revascularized after CA presented a significantly higher rate of risk factors and comorbidities and a 8-fold higher incidence of ischemic cerebrovascular events and a 3-fold increase in mortality during the index hospitalization. These differences, observed in our real-world registry, seem to be mainly due to substantial diverse baseline characteristics between the two groups.

In addition, these two distinct groups of patients seem to receive different pharmacological combinations. Indeed, in our registry LMWH and clopidogrel were mainly used among medically managed patients who did not undergo CA compared to patients not revascularized after CA who more often received UFH and novel P2Y12 inhibitors during hospitalization. This different therapeutic strategy might be related to the different ischemic and bleeding profiles of the two populations, as reflected by the higher GRACE and CRUSADE risk score in the 'no CA' compared to the 'after CA' group, or to the tendency of clinicians to administer more potent drugs after knowing coronary anatomy.

In our analysis, less than 60% of patients treated conservatively received DAPT at discharge, although recommended from current guidelines (16,17). The major predictors of non-prescription of DAPT at discharge were reasonable clinical causes such as recurrence of bleeding events and a history of bleeding. In addition, as suggested by the multivariable analysis, it cannot be excluded that the low rate of DAPT used in our series could be partially related to a number of patients discharged with a planned surgical revascularization. The benefits of DAPT have been firstly demonstrated in the CURE trial, where among patients medically managed the use of clopidogrel in

association to aspirin was associated with a 20% relative risk reduction of the primary endpoint (18). These findings have been recently confirmed in a large, community-based cohort of ACS patients who were medically managed, where clopidogrel use was associated with a lower risk of death and MI, particularly among patients with NSTEMI (19).

Additionally, data on ticagrelor are available from a pre-specified analysis of the PLATO trial (20) that analyzed patients (28% of the total study population) initially scheduled for conservative treatment (although about 25% of them subsequently received percutaneous or surgical revascularization). In this analysis, the incidence of the primary endpoint (death, infarction, or stroke) was lower in the ticagrelor group as compared to the clopidogrel group, with a significant reduction in all-cause mortality (20). In a post-hoc analysis of the PLATO trial on NSTE-ACS patients (21) benefit of ticagrelor over clopidogrel in reducing ischemic events and total mortality was consistent with the overall PLATO trial, including the 48.4% patients managed without revascularization within the first 10 days after randomization. Despite this superiority over clopidogrel, in our survey ticagrelor has been used at discharge in only 13.3% of NSTE-ACS and 10.0% of STEMI patients. On the other hand, clopidogrel was the preferred oral antiplatelet agent, especially among patients not undergoing CA. Prasugrel has been used in a small minority of patients probably based on the results from the TRILOGY ACS (Targeted Platelet Inhibition to Clarify the Optimal Strategy to Medically Manage Acute Coronary Syndromes) trial (22) where it was not associated with any clinical benefits as compared to clopidogrel. However, in a subsequent analysis of the TRILOGY ACS trial, the proportion of patients who reached the primary endpoint was lower in the prasugrel group than in the clopidogrel group for those who had CA but did not differ between groups in patients who did not have CA (23), confirming the different risk profile and derived benefits of these two groups of medically managed patients with ACS.

## CONCLUSIONS

In a contemporary cohort of ACS patients, almost one-third is managed conservatively during hospitalization. A higher risk of in-hospital events and lower rate of recommended antiplatelet therapy was observed in medically managed patients who do not undergo CA compared with those who receive a CA. These findings highlight the need for novel strategies to implement guidelines adherence in order to mitigate the increased risk of adverse outcomes in this population.

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**FIGURE LEGEND**

**Figure 1.** Medically managed patients enrolled in the EYESHOT study.

CA: coronary angiography

**Figure 2.** Independent predictors of not receiving coronary angiography during hospitalization

**Figure 3**. Independent predictors of conservative treatment after CA (excluding patients without significant stenoses at CA)

**Figure 4**. Antithrombotic therapies administered during hospitalization in 'no CA' and 'after CA' groups.

CA: coronary angiography; GP: glycoprotein; inhib.: inhibitors; LMWH: low-molecular weight heparins; UFH: unfractioned heparin

**Figure 5**. Incidence of in-hospital clinical events among STEMI and NSTE-ACS patients not undergoing CA or not revascularized after CA.

CA: coronary angiography; NSTE-SCA: Non-ST-elevation acute coronary syndromes; STEMI: ST-elevation myocardial infarction

## Appendix

### Steering Committee

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**Table 1.** Baseline clinical characteristics.

| | **Overall n=783** | **No CA n= 305** | **After CA n= 478** | **P value** |
|---|---|---|---|---|
| NSTE-ACS, n (%) | 649 (82.9) | 261 (85.6) | 388 (81.2) | 0.11 |
| Age, yrs (mean±SD) | 73±13 | 79±12 | 69±13 | <.0001 |
| ≥75 yrs old, n (%) | 394 (50.3) | 211 (69.2) | 183 (38.3) | <.0001 |
| Female, n (%) | 351 (44.8) | 155 (50.8) | 196 (41.0) | 0.007 |
| BMI (mean±SD) | 27±5 | 26±5 | 27±5 | 0.02 |
| GRACE risk score, median [IQR] | 159 [128-185] | 180 [155-206] | 145 [118-170] | <.0001 |
| CRUSADE risk score median [IQR] | 40 [25-52] | 50 [38-60] | 33 [20-46] | <.0001 |
| **Risk factors and comorbidities, n (%)** | | | | |
| Familiar history of CAD * | 185 (31.9) | 58 (30.1) | 127 (32.8) | 0.50 |
| Active smokers | 135 (17.2) | 34 (11.2) | 101 (21.1) | 0.0003 |
| Dyslipidemia* | 368 (53.8) | 137 (53.1) | 231(54.2) | 0.77 |
| Diabetes mellitus | 278 (35.5) | 120 (39.3) | 158 (33.1) | 0.07 |
| Hypertension | 600 (76.6) | 254 (83.3) | 346 (72.4) | 0.0004 |
| Renal dysfunction/dyalisis | 182 (23.2) | 103 (33.8) | 79 (16.5) | <.0001 |
| Severe COPD | 64 (8.2) | 32 (10.5) | 32 (6.7) | 0.06 |
| Malignancy | 28 (3.6) | 20 (6.6) | 8 (1.7) | 0.0003 |
| **Cardiovascular history, n (%)** | | | | |
| Peripheral artery disease* | 154 (21.2) | 77 (27.4) | 77 (17.3) | 0.001 |
| Previous stroke/TIA | 102 (13.0) | 60 (19.7) | 42 (8.8) | <.0001 |
| History of angina | 134 (17.1) | 67 (22.0) | 67 (14.0) | 0.004 |
| History of major bleed | 91 (11.6) | 53 (17.4) | 38 (8.0) | <.0001 |
| History of heart failure | 78 (10.0) | 59 (19.3) | 19 (4.0) | <.0001 |
| Previous MI | 227 (29.0) | 110 (36.1) | 117 (24.5) | 0.0005 |
| Previous PCI | 164 (21.0) | 66 (21.6) | 98 (20.5) | 0.70 |
| Previous CABG | 83 (10.6) | 46 (15.1) | 37 (7.7) | 0.001 |

* percentages evaluated on pts with data available

BMI: body mass index; CA: coronary angiography; CABG: coronary artery by-pass grafting; CAD: coronary artery disease; COPD: chronic obstructive pulmonary disease; MI: myocardial infarction; NSTE-ACS: Non-ST-elevation acute coronary syndromes; PCI: percutaneous coronary intervention; Revasc.: revascularization; TIA: transient ischemic attack.

**Table 2.** Hemodynamic parameters, laboratory variables and pharmacological therapy at baseline.

| | **Overall n=783** | **No CA n= 305** | **After CA n= 478** | **P value** |
|---|---|---|---|---|
| Killip class III-IV, n (%) | 100 (12.8) | 64 (21.0) | 36 (7.5) | <.0001 |
| SBP, mmHg (mean±SD) | 138±27 | 137±29 | 138±25 | 0.50 |
| HR, bpm (mean±SD) | 81±20 | 85±22 | 79±19 | 0.0001 |
| Ejection fraction, % (mean±SD) | 49±11 | 46±11 | 50±11 | <.0001 |
| Atrial fibrillation, n (%) | 89 (11.4) | 57 (18.7) | 32 (6.7) | <.0001 |
| Hb, gr/dl (mean±SD) | 12.8±2.1 | 12.1±2.2 | 13.1±1.9 | <.0001 |
| Glycemia, mg/dl (mean±SD) | 150±80 | 166±91 | 140±71 | <.0001 |
| Platelet count, x1000 (mean±SD) | 235.8±77.9 | 235.3±84.8 | 236.1±73.2 | 0.90 |
| **Antithrombotic treatment at baseline, n (%)** | | | | |
| ASA | 374 (47.8) | 172 (56.4) | 202 (42.3) | 0.0001 |
| Clopidogrel | 95 (12.1) | 45 (14.8) | 50 (10.5) | 0.07 |
| Ticlopidine | 28 (3.6) | 15 (4.9) | 13 (2.7) | 0.11 |
| Prasugrel | 8 (1.0) | 2 (0.7) | 6 (1.3) | 0.49 |
| Ticagrelor | 14 (1.8) | 6 (2.0) | 8 (1.7) | 0.76 |
| LMWH | 24 (3.1) | 15 (4.9) | 9 (1.9) | 0.02 |
| OAT | 49 (6.3) | 25 (8.2) | 24 (5.0) | 0.07 |

ASA: acetylsalicylic acid; CA: coronary angiography; Hb: hemoglobin; HR: heart rate; LMWH: low-molecular weight heparins; OAT: oral anticoagulation therapy; Revasc.: revascularization; SBP: systolic blood pressure.

**Table 3.** Antithrombotic therapies prescribed at discharge among medically managed patients discharge alive with a final diagnosis of STEMI or NSTE-ACS

| | **STEMI** | | | **NSTE-ACS** | | |
|---|---|---|---|---|---|---|
| | **No CA n=39** | **After CA n=81** | **P value** | **No CA n=242** | **After CA n=384** | **P value** |
| ASA, n (%) | 29 (74.4) | 74 (91.4) | 0.01 | 204 (84.3) | 350 (91.2) | 0.009 |
| Clopidogrel, n (%) | 25 (64.1) | 40 (49.4) | 0.13 | 144 (59.5) | 157 (40.9) | <.0001 |
| Ticlopidine, n (%) | 0 (0) | 0 (0) | - | 3 (1.2) | 2 (0.5) | 0.38 |
| Ticagrelor, n (%) | 0 (0) | 12 (14.8) | 0.009 | 26 (10.7) | 57 (14.8) | 0.14 |
| Prasugrel, n (%) | 0 (0) | 1 (1.2) | 1.0 | 1 (0.4) | 9 (2.3) | 0.10 |
| DAPT, n (%) | 22 (56.4) | 50 (61.7) | 0.58 | 156 (64.5) | 211 (55.0) | 0.02 |
| OAT, n (%) | 1 (2.6) | 8 (9.9) | 0.27 | 21 (8.9) | 27 (7.0) | 0.45 |

ASA: acetylsalicylic acid; CA: coronary angiography; DAPT: dual antiplatelet therapy; Revasc.: revascularization: OAT: oral anticoagulant therapy

**FIGURE 1**

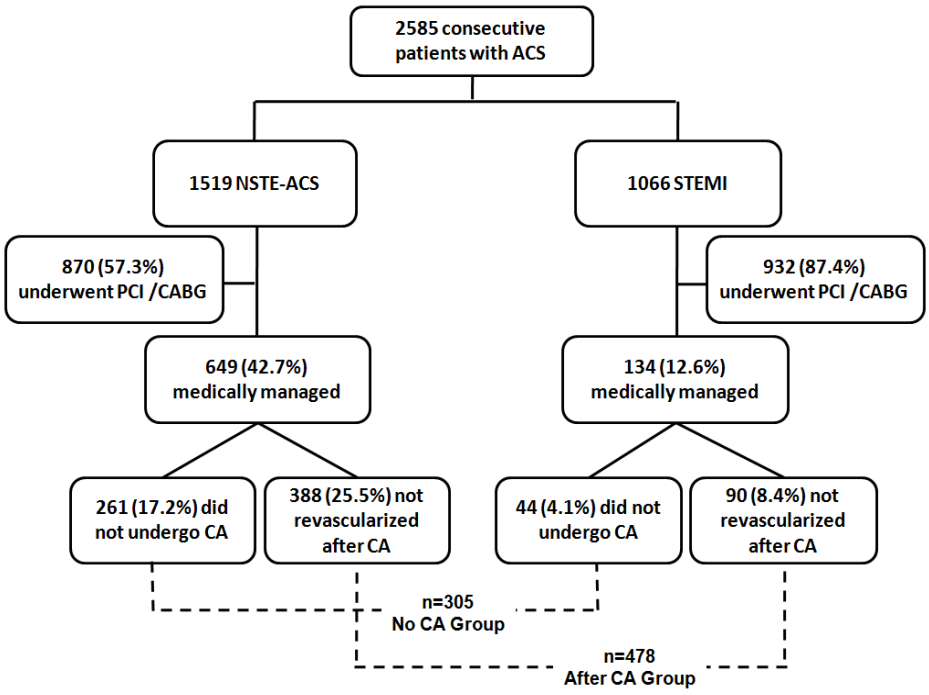
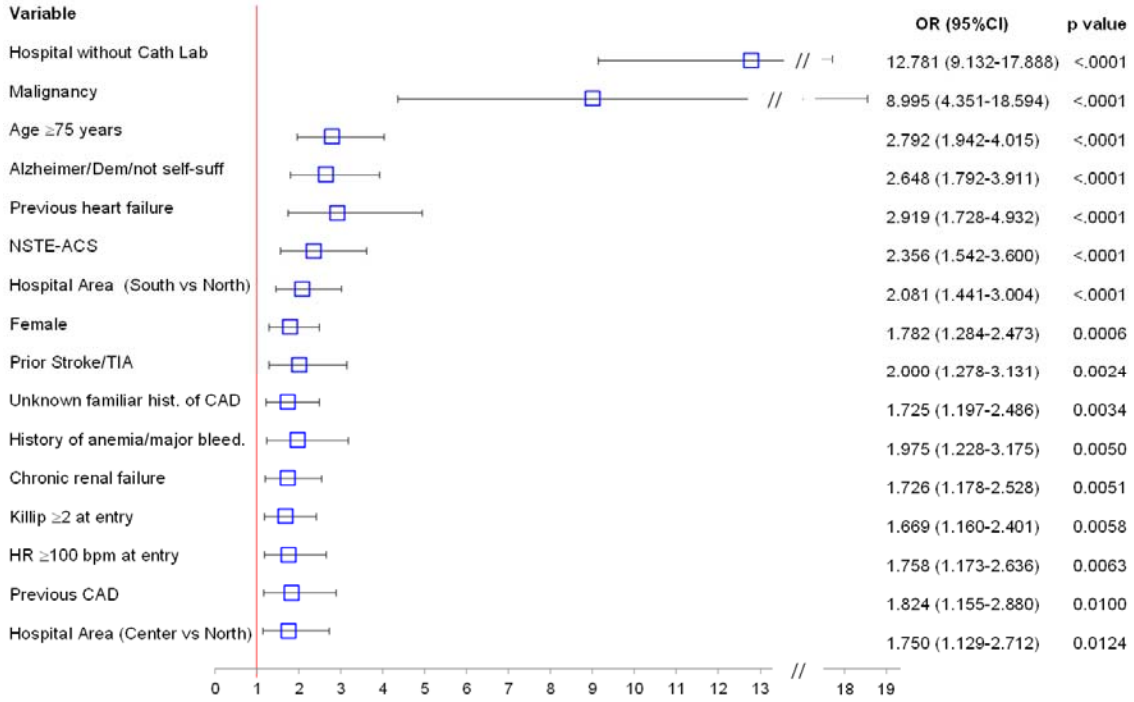
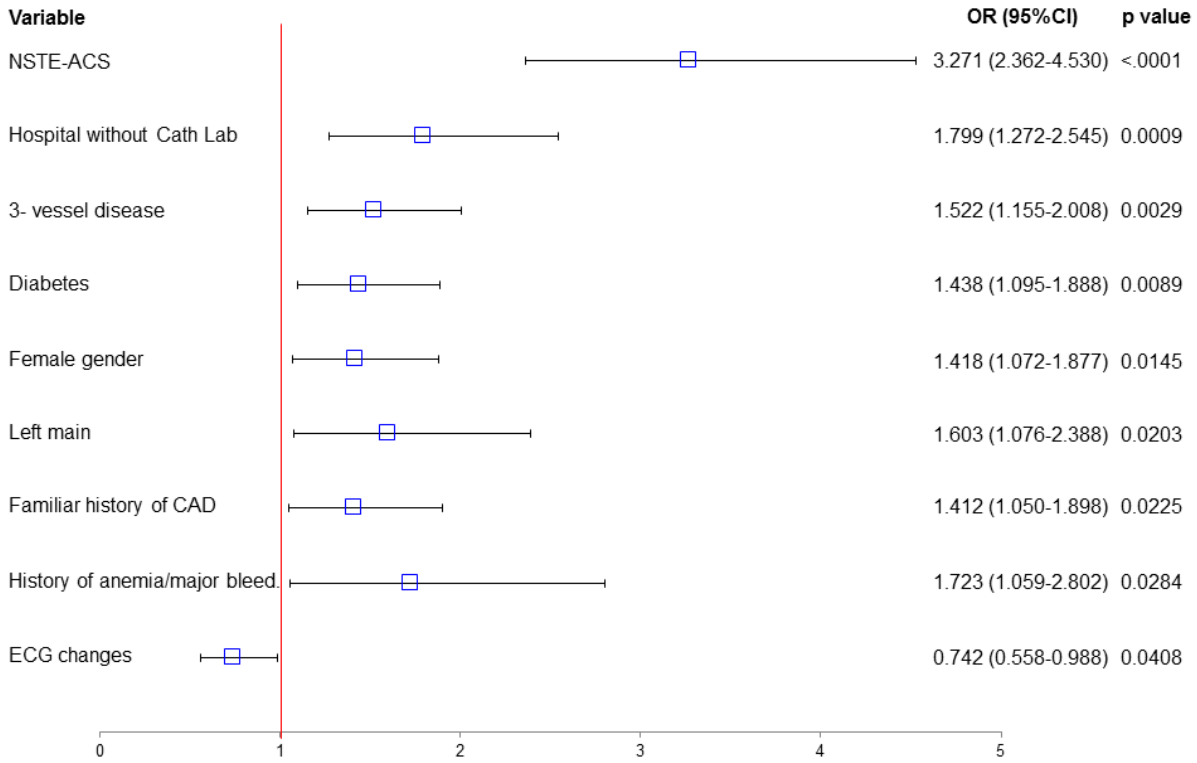

2585 consecutive patients with ACS
1519 NSTE-ACS
1066 STEMI
870 (57.3%) underwent PCI /CABG
932 (87.4%) underwent PCI /CABG
649 (42.7%) medically managed
134 (12.6%) medically managed
261 (17.2%) did not undergo CA
388 (25.5%) not revascularized after CA
44 (4.1%) did not undergo CA
90 (8.4%) not revascularized after CA
n=305 No CA Group
n=478 After CA Group

**FIGURE 2**




Variables included in the logistic regression model: sex, age ≥75 years, hypertension, diabetes, dyslipidemia (yes; no; unknown. No as reference), familiar history of coronary artery disease (CAD) (yes; no; unknown. No as reference), active smoker, previous stroke/transient ischemic attack (TIA), history of anemia/major bleedings, peripheral vascular disease (PVD) (yes; no/unknown as reference), chronic renal failure, malignancy, chronic obstructive pulmonary disease (COPD), Alzheimer/dementia/not self-sufficient, previous CAD, previous heart failure, previous revascularization, heart rate (HR) ≥100 bpm at entry, electric instability, ejection fraction ≤40% at entry, ECG changes, killip class ≥2 at entry, hospital without Cathlab, geographic area of the hospital (North; Center; South. North as reference), diagnosis at admission (NSTE-ACS vs STEMI).

**FIGURE 3**




Variables included in the logistic regression model: sex, age ≥75 years, hypertension, diabetes, familiar history of coronary artery disease (CAD) (yes; no; unknown. No as reference), active smoker, previous stroke/transient ischemic attack (TIA), history of anemia/major bleedings, peripheral vascular disease (PVD) (yes; no/unknown as reference), chronic renal failure, previous CAD, previous revascularization, electric instability, ECG changes, hospital without Cathlab, diagnosis at admission (NSTE-ACS vs STEMI), hospital admission between 8/20 h working days, left main, extent of CAD (1-2 vessel; 3 vessel. 1-2 vessel as reference)

**FIGURE 4**

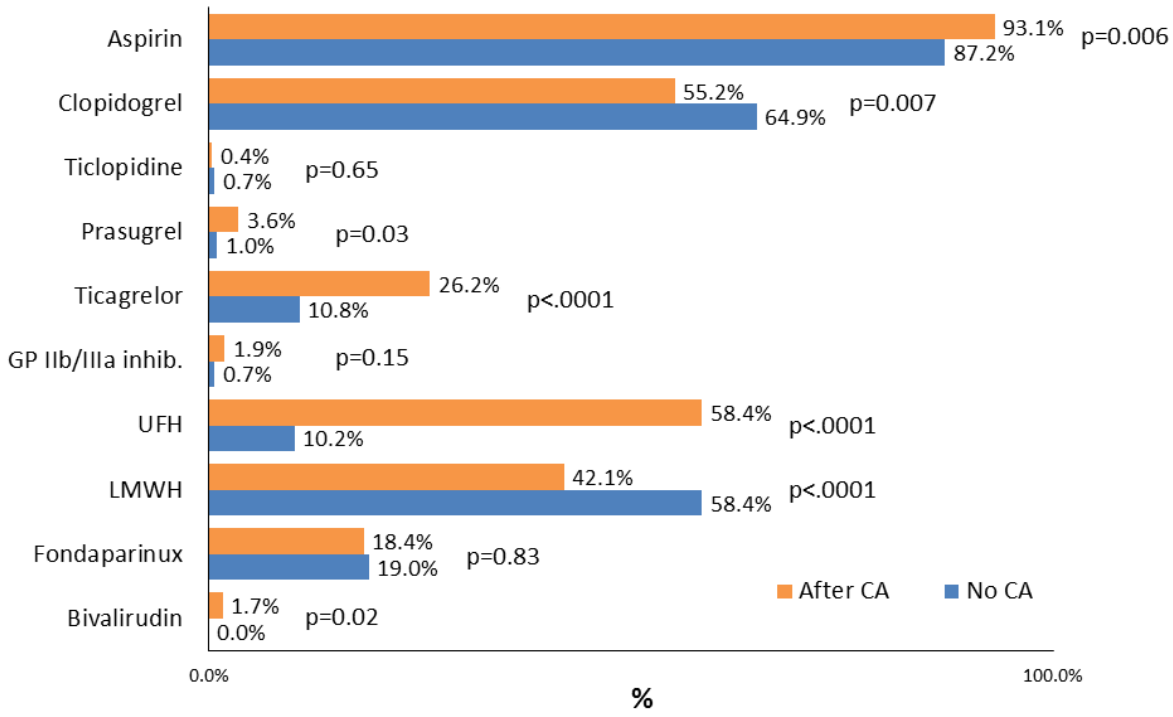
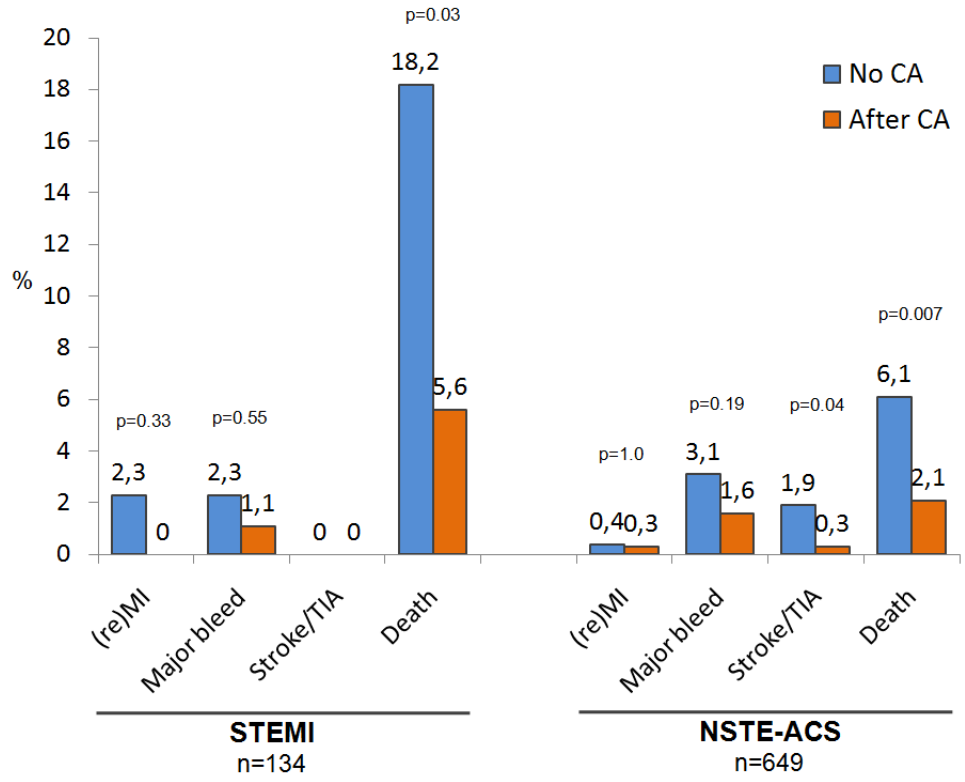

Aspirin
93.1%
87.2%
p=0.006
Clopidogrel
55.2%
64.9%
p=0.007
Ticlopidine
0.4%
0.7%
p=0.65
Prasugrel
3.6%
1.0%
p=0.03
Ticagrelor
26.2%
10.8%
p<.0001
GP IIb/IIIa inhib.
1.9%
0.7%
p=0.15
UFH
58.4%
10.2%
p<.0001
LMWH
42.1%
58.4%
p<.0001
Fondaparinux
18.4%
19.0%
p=0.83
Bivalirudin
1.7%
0.0%
p=0.02
After CA
No CA
0.0%
100.0%
%

**FIGURE 5.**


p=0.03
20
18
16
14
12
%
10
8
6
4
2
0
18,2
No CA
After CA
5,6
p=0.33
p=0.55
2,3
2,3
1,1
0
0
0
p=0.007
6,1
p=0.19
p=0.04
p=1.0
3,1
2,1
1,6
1,9
0,4
0,3
0,3
(re)MI
Major bleed
Stroke/TIA
Death
(re)MI
Major bleed
Stroke/TIA
Death
STEMI
n=134
NSTE-ACS
n=649