The British Cardiac Society Working Group
definition of myocardial infarction: implications for
practice

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Alistair S Hall¹ on behalf of the EMMACE-2 (Evaluation of Methods and Management
of Acute Coronary Events) Investigators*

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* EMMACE-2 Investigators listed in the appendix
The British Cardiac Society Working Group definition of myocardial infarction- implications for practice
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Objective: To assess the impact on observed mortality of the British Cardiac Society definition of myocardial infarction in 11 UK hospitals.

Design: Prospective observational registry.

Setting: 11 adjacent hospitals in the West Yorkshire region.

Patients: 2,484 patients with ACS were identified during a six-month window period (April 28th to October 28th 2003). Demographic, clinical and treatment variables were collected on all patients and their mortality status was monitored through the Office of National Statistics. Patients were categorised into 3 groups according to the BCS definition of MI: “ACS with unstable angina”; “ACS with myocyte necrosis” and “ACS with clinical MI”.

Results: 30-day mortality across the groups was 4.5%, 10.4% and 12.9% p<0.001 (ACS with unstable angina, ACS with myocyte necrosis and ACS with clinical MI respectively). At 6 months the mortality for patients in groups, “ACS with clinical MI” and “ACS with myocyte necrosis” were similar (19.2% vs. 18.7%) being higher than for “ACS with unstable angina” (8.6%). Same admission PCI was similar in groups with clinical MI and myocyte necrosis (11.1%, 10.7% respectively) as was CABG (2.6%, 2.7% respectively). However, there were significant differences between these two groups in the prescribing of secondary prevention (aspirin, statins, beta-blockers and ACE-inhibitors p<0.001).

Conclusions: At 30-days the new BCS categories for myocardial infarction predict three distinct outcomes. However, within a contemporary UK population this was no longer apparent at 6 months as mortality rates for patients with “ACS with myocyte necrosis” had risen to the same level as those for patients “ACS with clinical MI”. One possible explanation for this is the apparent under-use of drugs known to improve prognosis after traditional myocardial infarction.
BACKGROUND

In September 2000 the common disease state of myocardial infarction was redefined by the American College of Cardiology/European Society of Cardiology (ACC/ESC)[1]. Under this new definition, the measurement of cardiac troponins became the new gold standard for diagnosing myocardial injury. After years of applying the World Health Organisation (WHO) [2] [3] definition, scientists and health care providers alike, are only just beginning to come to terms with rapid developments in this area. The key areas of progress that have resulted in this change of definition are the ability to measure cardiac specific markers, cardiac troponin T (cTnT) and cardiac troponin I (cTnI) which are able to detect small amounts of myocardial necrosis and the widespread understanding that myocardial infarction and unstable angina generally represent a single heterogeneous disease state collectively renamed acute coronary syndrome (ACS).

Recently, the British Cardiac Society (BCS) Working Group commissioned a report [4]. The aims of the report were to help establish a consistent nomenclature on the definition of myocardial infarction, recommend a diagnostic threshold to distinguish patients with myocardial infarction (MI) from patients with other forms of acute coronary syndrome and to recommend a strategy for establishing a reference standard for troponin assays. Concern was raised regarding the fact that the ACC/ESC definition was overly dependent on the measurement of troponin despite significant lack of precision, accuracy and comparability among the assays currently available. Others have also made this criticism and highlighted the fact that no troponin assay currently available is able to fulfil the ACC/ESC requirements for a cut-off value at the 99th centile for a normal population while also with good precision indicated by a CV (coefficient of variation) of <10% [5,6,7]. In this context we aimed to explore the ease of use, demographic features, treatment and mortality rates associated when the BCS definition of MI was applied to a contemporary UK population of acute coronary syndrome patients.

PATIENTS AND METHODS

The study was designed as a prospective observational registry of patients admitted to 11 adjacent UK hospitals with ACS. Over a six-month period (April 28th to October 28th 2003) 6,715 potential cases of ACS were identified from the 11 UK hospitals. After evaluation of medical records, electrocardiograms and cardiac troponin and creatine kinase results, 2,499 confirmed cases of ACS were identified and recruited into the study. Potential ACS patients were identified from coronary care unit registers and from biochemistry lists of requests for cardiac troponin and creatine kinase measurement. All patients were included in the study regardless of age or medical/surgical speciality. The different search strategies were complimentary — that is, a significant number that were later validated would have been missed if only one of the search strategies, such as coronary care unit registers, had been employed. All patients regardless of age or consultant team were included in the study. The study was approved by a Multicentre Research Ethics Committee and the Local Research Ethics Committee from each local hospital. Written consent was obtained from patients to allow their medical notes to be evaluated and their health status to be monitored through the Office of Medical Statistics (ONS). Consent was also obtained to permit storage of a blood sample (taken routinely 12-24 hours after onset of symptoms) and for measurement of cardiac troponin (cTnI) together with other cardiac biomarkers.
Patients were potentially eligible if they were admitted to hospital either through casualty or directly to the ward with an admission diagnosis of suspected acute coronary syndrome. The judgement regarding appropriateness of inclusion was made by a Specialist Cardiology Research Nurses in conjunction with a Cardiology Research Registrar (RD & NK) also taking into account the views and opinions of the attending medical team. This was based firstly on clinical context and secondly on the results of cardiac biomarkers. Specifically, patients were included in the study if they fulfilled a revised ESC/ACC definition of myocardial infarction: Raised cardiac troponin value above the 10% CV taken 12-24 hours after the onset of symptoms OR raised CK value above 2 x ULN - Accompanied by at least one of the following – (i) ischaemic symptoms (ii) development of pathological Q waves on the ECG (iii) ECG changes indicative of ischaemia (iv) delivery of primary coronary angioplasty (v) compatible postmortem findings. Furthermore we included patients diagnosed as having acute coronary syndrome (ACS) on clinical grounds (i.e. clinical history, examination, ECG, angiography or post-mortem findings) when biomarkers were not available (e.g. due to very early death) and also when troponin values were negative based on the 10% CV threshold. Patients were excluded if they refused consent or if they were judged not to have a diagnosis of acute coronary syndrome. Our intention was to include a wide range of consenting “real world” acute coronary syndrome patients into the study.

A 150 item case record form listing demographic, clinical, and treatment variables was completed for each patient according to a standardised operations manual, and entered onto a computer database. Only one event was included (the first presentation with an ACS during the recruitment window), and patients transferred into a tertiary centre were counted only once for the index admission. Clinical characteristics on admission were taken from the following sources in order of preference: emergency department medical notes, admitting medical team’s first clerking, and nursing notes.

Data was abstracted from the medical notes by ten experienced research nurses and two cardiology registrars (RD & NK). The quality of data abstraction from case notes and data entry into the computer database was formally assessed. Data checks for completeness and consistency were performed and queries generated at regular intervals during the course of the study. In 55% of randomly generated cases, double-data entry was performed for key fields. All 11 centres were visited to confirm that screening methods and source data were adequate.

Patients were categorised into 3 groups according to the BCS definition using the following criteria:
- ACS with unstable angina (UA) (Accu Tn I ≤0.06 µg/L; 10% CV)
- ACS with myocardial necrosis (Accu Tn I > 0.06-0.5 µg/L)
- ACS with clinical MI (Accu Tn I > 0.5 µg/L or creatinine kinase twice the upper limit of normal of the reference range).

Patients were allocated groups by two cardiology registrars (RD & NK) and a consultant cardiologist (ASH) using data available from clinical history, serial ECGs and cardiac troponin and creatine kinase results.
Biochemical analysis of cTnI was performed using the Beckman Coulter Ltd. AccuTnI assay using an immunometric technique. Cardiac troponin was measured in six local hospital laboratories routinely using the Accu TnI assay and at a central core laboratory (Leeds General Infirmary) for 5 other local hospitals. For the purpose of this study we used the 10% CV value for the assay, which corresponds to an Accu Tn I result of 0.06ng/ml. Accu Tn I measurement was carried out in 1,975 patients and for the remaining 509 patients creatine kinase (CK) was measured as part of the patients routine care. The 509 patients who did not have a cTnI measured were identified on the basis of either ST elevation on the presenting ECG or a CK two times the upper limit of normal. A CK value of 400 U/L (2 times the upper limit of normal) was used as the MI diagnostic threshold. Current local guidelines within West Yorkshire indicate that patients with ST-elevation myocardial infarction (STEMI) do not require a cardiac troponin measurement to confirm a diagnosis. A diagnosis of STEMI can be based from clinical history, ECG changes and from creatinine kinase results.

Statistical analysis was performed using SPSS system 11.1 (SPSS Inc, Chicago, Illinois, USA) software. Continuous variables are presented as means (SD) and categorical variables as frequencies. Groups were compared using the chi-squared test for categorical data and analysis of variance (ANOVA) for continuous variables. Kaplan Meier analysis was used to analyse survival for patients in each of the 3 groups.

RESULTS
After evaluation of the medical records, 2,499 patients with ACS were confirmed. Using the BCS diagnostic criteria, cases were subsequently divided into 3 groups as follows: “ACS with unstable angina” (11%), “ACS with myocardial necrosis” (21%) and “ACS with clinical MI” (68%). In 15 patients it was not possible to determine a BCS category due to the fact that these patients died in hospital before any cardiac markers were measured, with no diagnostic ECG nor post-mortem findings. These patients were excluded from the analysis.

Demographic and clinical baseline characteristics for the BCS groups are given in Table 1. Patients having “ACS with myocyte necrosis” tended to be older and were more likely to be female (p<0.001) than the other groups. There was also a trend for “ACS with unstable angina” patients to have a previous history of AMI and hypercholesterolemia (defined as a serum cholesterol >5.1mmol/L before any statin therapy) as compared with the other groups (p<0.001). Patients having “ACS with clinical MI” were also more likely to be current smokers as compared to the other groups (p<0.001). A greater percentage of patients underwent PCI if they had “ACS with myocyte necrosis” or “ACS with clinical MI” (10.7% and 11.1% respectively) as compared to “ACS with unstable angina” (4.9%). This was found to be statistically significant (p=0.008).

The pharmacological treatment of patients admitted with ACS is shown in Table 2. In hospital use of low–molecular-weight-heparin was uniform across the groups (75% of cases) with a tendency to use unfractionated heparin in ACS patients with clinical MI. The use of clopidogrel was 44%, 55% and 52% (ACS with UA, ACS with myocardial necrosis, ACS with clinical MI, respectively). Only a small proportion of patients
received a Glycoprotein IIb/IIIa inhibitor as part of their in-hospital treatment (1% ACS with UA, 7% ACS with myocardial necrosis and 7% ACS with clinical MI). Intravenous nitrates were used more commonly in patients having “ACS with clinical MI” as compared to the other groups (p<0.001) and potassium channel modulators were used more frequently in patients having “ACS with UA” and “ACS with myocardial necrosis”. At discharge, there was an increase in secondary prevention prescribing across the groups. Patients having “ACS with clinical MI” were more likely to receive aspirin, beta-blockers, ACE-inhibitors and statins than compared to the other two groups (p<0.001).

Figure 1 shows Kaplan-Meier survival curves for the BCS definition groups. There was an observed increase in 30-day all-cause mortality rates across the groups (Log Rank Test, p<0.001). The mortality rates were as follows: 4.5%, 10.4% and 12.9% (“ACS with unstable angina”, “ACS with myocyte necrosis”, “ACS with clinical MI”, respectively). The six-month all-cause mortality was similar for patients having a diagnosis of “ACS with myocyte necrosis” and for those having a diagnosis of “ACS with clinical MI” (18.7% v 19.2%).

Patients having a diagnosis of “ACS with clinical MI” were further classified into NSTEMI and STEMI using serial ECGs together with cardiac troponin and CK results. The presence of ST elevation or bundle-branch block and an appropriate rise in biomarker(s) was used to distinguish those events categorized as STEMs. NSTEMI events included all other ECG patterns together with an appropriate rise in biomarker(s). The mortality at 30-days was 11.8% for NSTEMI and 14.4% for STEMI patients while at six months the mortality was identical for patients having “ACS with myocyte necrosis”, NSTEMI or STEMI (18.7%, 19.1% and 19.2%).

DISCUSSION
Previous studies have shown that patients identified by troponin elevations but normal creatinine kinase have a worse six-month outcome than do patients with MI defined by conventional criteria [8]. This observation has very important pathological and clinical implications as it suggests that patients with “ACS with myocyte necrosis” are at greater risk of re-infarction / completion of infarction. Consequently, patients with “ACS with myocyte necrosis” merit treatment and investigation strategies that are at least as aggressive as those given to patients with “ACS with clinical MI” [9]. In addition to other treatments, the Task Force on the Management of Acute Coronary Syndromes of the European Society of Cardiology advocate angiography and treatment with glycoprotein IIb/IIIa inhibitors for all patients with ACS and detectable troponin elevations but without ST elevation on the admission ECG. This group also advocate wider treatment with the same four drugs (aspirin, beta-blockers, statins, ACE-inhibitors) proven to be effective in secondary prevention following NSTEMI / STEMI. Routine administration of these drugs to patients previously classified as having unstable angina – cannot be directly supported by the randomised clinical trial evidence-base, yet is viewed by this and other groups as an important strategy for risk reduction.

In a contemporary UK cohort of patients, we have both confirmed and further extended the observation of delayed increases in total-mortality for patients with NSTEMI by showing that a similar effect is seen also for patients referred to as “ACS with myocyte necrosis”. The increase in total mortality between 30 and 180 days
was highest for this initially intermediate risk group (8.3% as compared to 4.1% & 6.3% for the other two groups). At 30-days all-cause mortality of patients with “ACS and unstable angina” is distinct from that seen for “ACS with myocyte necrosis” and “ACS with clinical MI” (4.5%, 10.4% and 12.9%, respectively). By 6 months the mortality of patients having “ACS with myocyte necrosis” is seen to rise to the same level as for “ACS with clinical MI” (18.7% and 19.2%, respectively) despite presumed lower levels of myocyte necrosis during the index event. Consequently, this paper represents the first report regarding the survival outcomes for patients that have been categorised using the new BCS Working Group MI terminology [4].

The evidence suggests that cardiac troponin levels correlate with mortality in patients with ACS [10]. With this in mind, one would expect ACS patients with lesser degrees of troponin elevation (“ACS with myocardial necrosis”) to have a lower mortality as compared to ACS patients with higher degrees of troponin elevation (“ACS patients with clinical MI”). As stated above, this observation was not seen in our cohort where total mortality at 6 months was the same for patients with “ACS with myocardial necrosis” and “ACS with clinical MI”. The likely explanation for this is later recurrence / completion of the infarction process in the group with initial evidence of more limited myocyte necrosis. However, we also observed a more conservative approach with regard to the use of secondary prevention (aspirin, beta-blockers, statins and ACE-inhibitors) in managing patients having a diagnosis of “ACS with myocardial necrosis” as compared to “ACS with clinical MI”. This strongly suggests one key strategy for improving the outcome of these patients. It must be acknowledged that there were also important baseline differences between the groups, which could partially account for these results. For example “ACS with myocyte necrosis” patients tended to be older, female, had higher heart rate and a previous history of myocardial infarction as compared to “ACS with clinical MI” which could contribute to this ‘catch up’ phenomenon at six months.

Our study also highlights that case fatality rates at 6 months were higher than in the multinational GRACE population [11]. One potential reason for this is that the mean age was just 66 years (i.e. 4 years younger) and also coronary angiography and percutaneous coronary intervention (PCI) rates in GRACE were much higher (STEMI; angiography = 55% & PCI = 53%; NSTEMI = 42% & 40%; UA = 28% & 18%) as compared to EMMACE-2 patients (ACS with clinical MI = 24% and 28%; ACS with myocardial necrosis = 21% and 11%; and ACS with UA = 11% and 5%). This suggests scope for improvement in the availability and delivery of the invasive approach to the management our ACS patients as supported by the FRISC-II and TACTICS trials and in line with both US and European guidelines [9][12][13][14]. Such an approach is supported by a recent meta-analysis and review of literature which demonstrates that a routine invasive approach reduces mortality in the setting of UA / NSTEMI and also primary PCI for STEMI patients [15][16].

In addition to assessment of differences in the use of drugs capable of secondary prevention and also the frequency of use of more interventional strategies, we evaluated the use of newer, evidence-based, anti-thrombotic treatments in the acute management of ACS patients [9][14][17][18]. Despite the advice of UK (NICE) and European authorities based on evidence to support greater use of glycoprotein IIb/IIIa inhibitors in ACS, [9][19] only a small proportion of patients received this treatment in hospital (7% “ACS with clinical MI”, 7% “ACS with myocardial necrosis”
and 1% for “ACS with UA”). In contrast, the use of oral clopidogrel acutely and after discharge was better (51% & 39% for all ACS patients) being highest in patients having “ACS with myocardial necrosis” (55% and 42% acutely and after discharge). Nevertheless – there remains much scope for improvement also for this aspect of routine care.

The applicability of our results is limited by the fact that a double cut-off for troponin is proposed the BCS Working Group - the lowest to diagnose myocardial injury and the highest to diagnose myocardial infarction. The recommendations to revise the ACC/ESC definition suggest that an analytical target of 10% coefficient of variation (% CV) be used as a cut off when diagnosing myocardial injury. Furthermore, as this level varies considerably between different assays these is also a need for improvements in other aspects of assay performance. The 8.6% six month mortality seen in patients having “ACS with UA” emphasizes the need for better discrimination and triage of ACS patients at this end of the spectrum.

For most troponin assays, little is known about the amount of troponin elevation which corresponds to a CK or CK-MB elevation that would satisfy the WHO MI definition [2] [3]. Indeed in the BCS paper (that takes into consideration only one of several troponin I assays which are currently available) only a personal communication is quoted to determine the cut off level for troponin I corresponding to CK or CK-MB elevation that would satisfy the WHO criteria [4]. However, this higher ‘cut-off’ is of much less clinical relevance if patients having “ACS with MI” and “ACS with myocyte necrosis” are treated in a much more similar manner than is current practice.

Definite myocardial infarction was previously defined as the combination of two of three characteristics: typical symptoms of infarction (that is, chest pain or discomfort), a rise in plasma or serum cardiac enzymes, and a typical ECG pattern involving the development of Q waves [2]. However, there was also the potential to classify a clinical event as being either a “Probable” or “Possible” myocardial infarction. In 2000 the American College of Cardiology (ACC) and the European Society of Cardiology (ESC) redefined the diagnostic criteria for MI to include the measurement of cardiac troponin as a diagnostic indicator of myocardial injury [1]. This change in definition has meant that patients previously diagnosed as having unstable angina may now be classified as having a myocardial infarction according to ACC/ESC definition [1]. The adoption of ACC/ESC definition has been shown to cause a doubling in the number of patients classified as having a myocardial infarction [20]. These additional patients who were previously classified as unstable angina patients tend to be older, have greater comorbidities and a less favourable outcomes as compared to WHO MI patients [8] [20]. As this definition has an impact on a wide range of other factors (e.g. guidelines, treatment pathways, epidemiological monitoring) and because there are practical challenges in the use of imperfect troponin assays – implementation has been variable and incomplete and has given rise to new complexity and confusion. This suggests the need for an interim or transition period between old and new definitions.

In this study we have investigated the implications of the new BCS definition of myocardial infarction in a contemporary UK cohort. We have identified a group of patients defined as having ‘ACS with myocardial necrosis’ to have the same mortality...
at six months as those patients classified as ‘ACS with clinical MI’ despite having lesser degrees of cardiac muscle damage. In the context of previous definitions of MI: ‘ACS with clinical MI’ represent patients previously classified as WHO MI [2] & ‘ACS with myocardial necrosis’ represents patients previously classified as having unstable angina. Together these two categories fulfil a revised ACC/ESC definition for myocardial infarction [1,5,6,7]. However, until an identical range of treatments are routinely given to patients within the different methods of categorization (ACC/ESC definition MI; BCS definition MI; WHO definition MI) it is impossible to assess the mortality associated with each of these various definitions.

In conclusion, we have looked in detail at ease of application and also clinical usefulness of the newly proposed BCS definition of myocardial infarction. We have assessed differences in treatment received and the associated short and long-term mortality for a ‘real world’ UK cohort. Our findings support the value of a revised (use of 10% CV as diagnostic cut-off) ACC/ESC definition of MI as the additional cohort of patients now diagnosed as having had an MI, have a prognosis identical to those covered by the old definition. The relatively limited use of interventional strategies, acute and secondary prevention drugs, further suggest that in particular, patients with myocardial necrosis might benefit both from early identification and also from being treated more aggressively than at present.

The new British Cardiac Society recommendations regarding ACS classification were found to be very practical by simultaneously allowing identification of patients previously categorized as having either MI or unstable angina while at the same time covering the new extended definition (ACC/ESC 2000) for myocardial infarction. This is of great help during the transition from one definition to the other as many clinical guidelines, care pathways, clinical trials, epidemiology studies - have yet to fully respond to a change of definition. Furthermore, the identification of a category of ACS patients with unstable angina, on clinical but not biochemical grounds, allows additional focus to be brought to the inadequacies of current diagnostic strategies. Additional research into the concomitant use of alternate diagnostic assays and also the development of better troponin assays is to be strongly encouraged as the 6 month mortality (8.6%) for this form of ACS is also high.
ETHICAL APPROVAL – The study was approved by the Eastern Multi-Research Ethics Committee and the Local Research Ethics Committees within West Yorkshire.

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TABLE LEGENDS

Table 1. Baseline characteristics

Table 2. Pharmacological treatments during Hospital Stay and at Discharge

FIGURE LEGENDS

Figure 1. Panel A shows 30-day mortality according to BCS category. Panel B shows Kaplan-Meier survival curves for events from admission to 6 months.
REFERENCES


APPENDIX: STRUCTURE OF THE EMMACE-2 STUDY GROUP

Principal Investigator – Alistair S Hall

Co-Supervisors – Michael B Robinson (Public Health) & Julian H Barth (Clinical Biochemistry)

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Nurse Co-ordinator – Christine Morrell

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Statistical analysis – Alistair S Hall, Rajiv Das & Niamh Killcullen

Database Management – Peter Tooze

Key Investigators – M Appleby, W Baig, SG Ball, PD Batin, KE Berkin, JM Blaxill, T Bloomer, WP Brooksby, JC Cowan, R Crook, C Dickinson, S Grant, H Larkin, RV Lewis, S Lindsey, AF Mackintosh, J Mclenachan, S McGerrary, LCA Morley, GW Morrison, CB Pepper, EJ Perrins, MM Pye, G Reynolds, RJ Sapsford, NP Silverton, JH Smyllie, RN Stevenson, LB Tan, CJP Welsh, GJ Williams, JI Wilson, AV Zezulka
**Table 1. Baseline Characteristics**

<table>
<thead>
<tr>
<th>British Cardiac Society Category</th>
<th>ACS with unstable angina n=268</th>
<th>ACS with myocyte necrosis n=530</th>
<th>ACS with Clinical MI n=1,686</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age, years (SD)</td>
<td>69.1 (12.8)</td>
<td>71.8 (12.6)</td>
<td>69.7 (13.3)</td>
<td>0.03</td>
</tr>
<tr>
<td>Female</td>
<td>89 (33%)</td>
<td>241 (46 %)</td>
<td>601 (36%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Current Smoker</td>
<td>51 (19%)</td>
<td>114 (22%)</td>
<td>509 (30%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Systolic BP (mm Hg)</td>
<td>142.1 (27.2)</td>
<td>144.2 (30.5)</td>
<td>141.4(30.4)</td>
<td>NS</td>
</tr>
<tr>
<td>Heart Rate (beats per minute)</td>
<td>79.9 (23.0)</td>
<td>87.9 (25.4)</td>
<td>83.3 (23.4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Past Medical History</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AMI</td>
<td>97 (36%)</td>
<td>155 (29%)</td>
<td>373 (22%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hypertension</td>
<td>133 (50%)</td>
<td>233 (44%)</td>
<td>696 (41%)</td>
<td>NS</td>
</tr>
<tr>
<td>Diabetes Mellitus</td>
<td>52 (19%)</td>
<td>94 (18%)</td>
<td>280 (17%)</td>
<td>NS</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>125 (47%)</td>
<td>197 (37%)</td>
<td>514 (31%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Peripheral vascular disease</td>
<td>25 (9%)</td>
<td>51 (10%)</td>
<td>32 (8%)</td>
<td>NS</td>
</tr>
<tr>
<td>Same admission</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Angiogram</td>
<td>55 (21%)</td>
<td>146 (28%)</td>
<td>403 (24%)</td>
<td>NS</td>
</tr>
<tr>
<td>PCI</td>
<td>13 (5%)</td>
<td>56 (11%)</td>
<td>187 (11%)</td>
<td>0.008</td>
</tr>
<tr>
<td>CABG</td>
<td>6 (2%)</td>
<td>14 (3%)</td>
<td>44 (3%)</td>
<td>NS</td>
</tr>
<tr>
<td>Planned</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Angiogram</td>
<td>16 (6%)</td>
<td>29 (6%)</td>
<td>123 (7%)</td>
<td>NS</td>
</tr>
<tr>
<td>PCI/CABG</td>
<td>7 (3%)</td>
<td>23 (4%)</td>
<td>67 (4%)</td>
<td>NS</td>
</tr>
<tr>
<td>All-cause Mortality</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>30 day</td>
<td>4.5%</td>
<td>10.4%</td>
<td>12.9%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>6 month</td>
<td>8.6%</td>
<td>18.7%</td>
<td>19.2%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Increase 30 day to 6 month</td>
<td>4.1%</td>
<td>8.3%</td>
<td>6.3%</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
Table 2. Pharmacological treatments during hospital stay and at discharge

<table>
<thead>
<tr>
<th></th>
<th>ACS with unstable angina (n=268)</th>
<th>ACS with myocardial necrosis (n=530)</th>
<th>ACS with clinical MI (n=1,686)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>IN HOSPITAL</strong></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Unfractionated heparin</td>
<td>8 (3%)</td>
<td>23 (4%)</td>
<td>252 (15%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Low mol. weight heparin</td>
<td>192 (72%)</td>
<td>401 (76%)</td>
<td>1230 (73%)</td>
<td>ns</td>
</tr>
<tr>
<td>Clopidogrel</td>
<td>118 (44%)</td>
<td>290 (55%)</td>
<td>866 (52%)</td>
<td>0.033</td>
</tr>
<tr>
<td>Glycoprotein IIb/IIIa inhibitor</td>
<td>3 (1%)</td>
<td>36 (7%)</td>
<td>121 (7%)</td>
<td>0.004</td>
</tr>
<tr>
<td>Intravenous beta-blocker</td>
<td>1 (0.4%)</td>
<td>5 (1%)</td>
<td>32 (2%)</td>
<td>ns</td>
</tr>
<tr>
<td>Calcium antagonists</td>
<td>77 (29%)</td>
<td>116 (22%)</td>
<td>319 (19%)</td>
<td>0.005</td>
</tr>
<tr>
<td>Intravenous nitrate</td>
<td>12 (5%)</td>
<td>56 (11%)</td>
<td>320 (19%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Oral nitrates</td>
<td>142 (53%)</td>
<td>262 (49%)</td>
<td>726 (43%)</td>
<td>0.007</td>
</tr>
<tr>
<td>Potassium channel modulator</td>
<td>62 (23%)</td>
<td>115 (22%)</td>
<td>227 (14%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>AFTER DISCHARGE</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Beta Blocker</td>
<td>139 (53%)</td>
<td>277 (53.1 %)</td>
<td>1106 (66%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Statin</td>
<td>181 (69%)</td>
<td>358 (68.5 %)</td>
<td>1350 (80%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ACE inhibitor</td>
<td>121 (46%)</td>
<td>276 (52.8 %)</td>
<td>1094 (65%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Aspirin</td>
<td>190 (72%)</td>
<td>362 (69.1 %)</td>
<td>1327 (79%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Clopidogrel</td>
<td>85 (32%)</td>
<td>224 (42.3%)</td>
<td>651 (39%)</td>
<td>0.004</td>
</tr>
</tbody>
</table>
Figure 1: Panel A shows 30-day mortality according to BCS category. Panel B shows Kaplan-Meier survival curves for events from admission to 6 months.