**AN ELECTRONIC ORDER SET FOR ACUTE MYOCARDIAL INFARCTION IS ASSOCIATED WITH BETTER ADHERENCE TO CLINICAL PRACTICE GUIDELINES AND IMPROVED PATIENT OUTCOMES**

APPENDIX 1: COMPONENTS OF THE ACUTE CORONARY SYNDROME ORDER SET

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**APPENDIX 1**

**COMPONENTS OF THE ACUTE CORONARY SYNDROME (AMI) ORDER SET (AMI-OS)**

Order set provides a list of required orders, medications, studies and consultation at the time of order initiation. The AMI Order Set was developed by a multidisciplinary expert panel based upon reviews of the literature and national guidelines.

Required Medications:

1. Aspirin 325 mg oral daily or 162mg oral daily

2. Metroprolol 25 mg oral twice a day or Atenolol 25 mg oral daily or Metoprolol 5mg IV

3. Lisinopril 5 mg oral daily or Captopril 12.5mg oral every 8 hours or Losartan oral 25mg daily

4. Atorvastatin 40 mg or 80 mg oral daily, or Pravastatin 20 or 80 mg oral daily or Simvastatin 40 mg oral daily

Optional Medications or Medications As Needed:

1. Clopidogrel 75 mg oral daily or 300mg oral single dose

2. Unfractionated heparin drip (weight based)

3. Enoxapin 1 mg/kg subcutaneous every 12 hours

4. Nitroglycerin 0.4 mg sublinguinal every 5 minutes or nitroglycerin 1 gm transdermal every 6 hours or nitroglycerin drip 20 mccg/minute IV infusion

5. Acetaminophen 650 mg oral every 4 hours for headache

6. Morphine Sulfate 2 mg IV every 5 minutes as needed

Laboratory Tests:

1. Chem 7 Panel (Serum testing for Sodium, Potassium, Chloride, BUN, Glucose, Creatinine, and Bicarbonate)

2. Lipid Panel (Serum testing for High Density Lipoproteins, Low Density Lipoproteins, Lipoprotein ratio, and Triglycerides)

3. Serum Troponin every 6 hours

4. Serum Alanine Aminotransferase (ALT)

5. Serum Prothrombin Time (PT) and International Normalized Ratio (INR)

6. Complete Blood Count (CBC) without Differential

Other Studies:

1. Electrocardiogram (ECG) daily and a Standing Order for additional ECG studies should the patient be noted as symptomatic by nursing staff

2. Chest X-Ray

3. Transthoracic Echocardiogram

Consultation:

Cardiology consultation is automatically initiated when the order set is opened. Upon signing by the physician, the system routes a communication to the cardiologist on service notifying of the consultation request.

**APPENDIX 2**

**STUDY COHORT ASSEMBLY**

During the study period, a total of 10,437 patients were potentially eligible to be included in our study. Of these, 982 were excluded because they were admitted after 2010 and LAPS2 data was not available for them, and 882 were excluded because KPHC was in operation for < 3 months at the hospital. Another 894 patients were excluded since they were not admitted for an overnight stay, 1,019 were excluded because the AMI-OS was used but it was not the first set of orders, and 772 were excluded because they were transfers from non-KPNC hospitals. Lastly, 58 patients were excluded as a result of manual chart review performed by two of us (Ballesca and Lee) because the diagnosis of AMI could not be confirmed. Characteristics of the remaining 5,879 eligible patients are summarized in Table 1 in the main text.

**APPENDIX 3**

|  |  |  |
| --- | --- | --- |
| LOGISTIC REGRESSION MODEL FOR INPATIENT MORTALITY (ORDER SET AND THERAPIES) | | |
| **Outcome** | **Death** |  |
| **Number of Outcomes** | *277* |  |
|  |  |  |
|  | **AOR1** | **95% CI2** |
| **Age in years** |  | |
| 18-39 | Ref |  |
| 40-64 | 1.01 | (0.13 - 7.68) |
| 65-84 | 3.93 | (0.53 - 28.98) |
| 85+ | 4.83 | (0.65 - 36.09) |
| **Sex** |  |  |
| Female | Ref |  |
| Male | 1.06 | (0.82 - 1.38) |
| **STEMI3** |  |  |
| Absent | Ref |  |
| Present | 3.75 | (2.56 - 5.49) |
| **Troponin I** |  |  |
| ≤0.1 ng/ml | Ref |  |
| >0.1 ng/ml | 1.07 | (0.76 - 1.50) |
| **COPS24** (AOR per 10 points) | 1.04 | (1.01 - 1.08) |
| **LAPS24** (AOR per 10 points) | 1.09 | (1.06 - 1.11) |
| **ED LOS5** (hours) |  |  |
| <6 | Ref |  |
| 6-7 | 0.75 | (0.54 - 1.06) |
| >=12 | 0.82 | (0.39 - 1.75) |
| **Code Status6** |  |  |
| Full Code | Ref |  |
| Not Full Code | 1.11 | (0.80 - 1.55) |
| **Cardiac Procedure Referral** |  |  |
| None during stay | Ref |  |
| 1 day pre adm until discharge | 0.38 | (0.28 - 0.53) |
| **Order Set Employed7** |  |  |
| No | Ref |  |
| Yes | 0.79 | (0.60 - 1.04) |
| **Aspirin Therapy** | 0.84 | (0.51 - 1.39) |
| **Anticoagulation Therapy** | 0.87 | (0.65 - 1.18) |
| **Beta Blocker Therapy** | 0.49 | (0.37 - 0.66) |
| **Statin Therapy** | 0.66 | (0.46 - 0.93) |
| **ACE8 inhibitors or ARB8s** | 0.41 | (0.31 - 0.54) |
| **C Statistic** | 0.823 |  |
| **Hosmer-Lemeshow p value** | 0.492 |  |

Footnotes to APPENDIX 3

1 Adjusted odds ratio

2 95% confidence interval

3 ST-segment elevation myocardial infarction present

4 See text and preceding table for details on COmorbidity Point Score, version 2 and Laboratory Acute Physiology Score, version 2.

5 Emergency department length of stay

6 See text for details on how care directives were categorized.

7 See text for details on order set

8 ACE = angiotensin converting enzyme; ARB = angiotensin receptor blockers.

**APPENDIX 4**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **DESCRIPTION OF STUDY COHORT (PROPENSITY MATCH)** | |  | |  |
|  |  | **Patients initially managed using** | | **P1** |
|  | **All Patients** | **AMI order set2** | **A la carte2 orders** |  |
|  | N=4,304 | N=2,152 | N=2,152 |  |
| **Age in years median(mean ± SD3)** | 71 ( 69.9 ± 13.6) | 71 ( 70.2 ± 13.5) | 70 ( 69.6 ± 13.7) | 0.1418 |
| **Age (% > 65 years)** | 2,697 ( 62.7%) | 1,367 ( 63.5%) | 1,330 ( 61.8%) | 0.2436 |
| **Sex (% male)** | 2,625 ( 61.0%) | 1,304 ( 60.6%) | 1,321 ( 61.4%) | 0.5952 |
| **STEMI4 (% with)** | 371 ( 8.6%) | 165 ( 7.7%) | 206 ( 9.6%) | 0.0260 |
| **Troponin I (% missing)** | 203 ( 4.7%) | 69 ( 3.2%) | 134 ( 6.2%) | <0.0001 |
| **Troponin I median(mean ± SD)** | 0.40 ( 2.7 ± 8.3) | 0.55 ( 2.9 ± 7.4) | 0.29 ( 2.6 ± 9.1) | 0.2572 |
| **Charlson Score5 median(mean ± SD)** | 3.0 ( 2.8 ± 1.6) | 3.0 ( 2.8 ± 1.6) | 3.0 ( 2.8 ± 1.6) | 0.1026 |
| **COPS26 median(mean ± SD)** | 21.0 ( 36.5 ± 35.3) | 23.0 ( 37.8 ± 35.9) | 18.0 ( 35.1 ± 34.7) | 0.0130 |
| **LAPS27 (median, mean ± SD)** | 27.0 ( 40.6 ± 47.2) | 29.0 ( 40.3 ± 46.4) | 26.0 ( 40.9 ± 48.0) | 0.6639 |
| **Length of stay in ED (hours) (median, mean ± SD)** | 5.7 ( 5.6 ± 2.7) | 5.7 ( 5.7 ± 2.3) | 5.70 ( 5.5 ± 3.1) | 0.1142 |
| **Patients receiving aspirin within 24 hours8** | 4,130 ( 96.0%) | 2,109 ( 98.0%) | 2,021 ( 93.9%) | <0.0001 |
| **Patients receiving anticoagulation therapy8** | 3,422 ( 79.5%) | 1,757 ( 81.6%) | 1,665 ( 77.4%) | 0.0005 |
| **Patients receiving beta blockers8** | 3,690 ( 85.7%) | 1,920 ( 89.2%) | 1,770 ( 82.3%) | <0.0001 |
| **Patients receiving ACE inhibitors or ARBs8** | 2,558 ( 59.4%) | 1,420 ( 66.0%) | 1,138 ( 52.9%) | <0.0001 |
| **Patients receiving statins8** | 3,843 ( 89.3%) | 2,015 ( 93.6%) | 1,828 ( 84.9%) | <0.0001 |
| **Patient received 1 or more therapies** | 4,289 (99.7%) | 2,152 (100.0%) | 2,137 (99.3%) | 0.0001 |
| **Patient received 2 or more therapies** | 4,221 (98.1%) | 2,143 (99.6%) | 2,078 (96.6%) | <0.0001 |
| **Patient received 3 or more therapies** | 4,006 (93.1%) | 2,087 (97.0%) | 1,919 (89.2%) | <0.0001 |
| **Patient received 4 or more therapies** | 3,317 (77.1%) | 1,803 (83.8%) | 1,514 (70.4%) | <0.0001 |
| **Patient received all 5 therapies** | 1,810 (42.1%) | 1,036 (48.1%) | 774 (36.0%) | <0.0001 |
| **Predicted mortality risk(%)9(median,mean ±SD)** | 1.2 ( 4.3 ± 9.5) | 1.1 ( 3.7 ± 7.9) | 1.2 ( 4.8 ± 10.8) | <0.0001 |
| **Full code at time of hospital entry10 (%)** | 3,732 ( 86.7%) | 1,859 ( 86.4%) | 1,873 ( 87.0%) | 0.5296 |
| **Admitted to ICU11 (%)** |  |  |  |  |
| **Direct admit (%)** | 1,081 ( 25.1%) | 572 ( 26.6%) | 509 ( 23.7%) | 0.0268 |
| **Unplanned Transfer (%)** | 278 ( 6.5%) | 152 ( 7.1%) | 126 ( 5.9%) | 0.1069 |
| **Ever (%)** | 1,854 ( 43.1%) | 864 ( 40.2%) | 990 ( 46.0%) | 0.0001 |
| **Length of stay (hours) (median, mean ± SD)** | 70.3 ( 114.3 ± 153.7) | 70.7 ( 113.3 ± 151.2) | 70.0 ( 115.2 ± 156.2) | 0.6842 |
| **Inpatient mortality (%)** | 235 ( 5.5%) | 96 ( 4.5%) | 139 ( 6.5%) | 0.0039 |
| **30 day mortality (%)** | 338 ( 7.9%) | 155 ( 7.2%) | 183 ( 8.5%) | 0.1126 |
| **All cause rehospitalization within 30 days (%)** | 790 ( 18.4%) | 413 ( 19.2%) | 377 ( 17.5%) | 0.1563 |
| **Cardiac cath procedure referral timing** |  |  |  |  |
| **1 day pre adm to disch** | 2,344 ( 54.5%) | 1,159 ( 53.9%) | 1,185 ( 55.1%) | 0.6860 |
| **2 days pre adm or earlier** | 163 ( 3.8%) | 77 ( 3.6%) | 86 ( 4.0%) |  |
| **After discharge** | 190 ( 4.4%) | 96 ( 4.5%) | 94 ( 4.4%) |  |
| **No referral** | 1,607 ( 37.3%) | 820 ( 38.1%) | 787 ( 36.6%) |  |

Footnotes to APPENDIX 4

1 Chi square or t test, as appropriate. See text for further methodological details.

2 AMI order set is an evidence-based electronic checklist which guides physicians to order the most effective therapy by CPOE during the hospital admission process. In contrast, a la carte means that the clinician did not use the AMI-OS , but rather entered individual orders via CPOE. See text for further details.

3 Standard deviation.

4 ST-segment elevation myocardial infarction as evident by electrocardiogram. See text for details on ascertainment.

5 See text and citation 31 for details on how this score was assigned.

6 COmorbidity Point Score, version 2. The COPS2 is a longitudinal, diagnosis-based score assigned monthly that integrates all diagnoses incurred by a patient in the preceding 12 months. It is a continuous variable that can range between a minimum of zero and a theoretical maximum of 1,014, although < 0.05% of Kaiser Permanente hospitalized patients have a COPS2 exceeding 241 and none have had a COPS2 > 306. Increasing values of the COPS2 are associated with increasing mortality. See text and citations 20 and 27 for additional details on the COPS2.

7 Laboratory-based Acute Physiology Score, version 2. The LAPS2 integrates results from vital signs, neurological status checks, and 15 laboratory tests in the 72 hours preceding hospitalization into a single continuous variable. Increasing degrees of physiologic derangement are reflected in a higher LAPS2, which can range between a minimum of zero and a theoretical maximum of 414, although < 0.05% of Kaiser Permanente hospitalized patients have a LAPS2 exceeding 227 and none have had a LAPS2 > 282. Increasing values of LAPS2 are associated with increasing mortality. See text and citations 20 and 27 for additional details on the LAPS2.

8 See text for details of specific therapies and how they were ascertained using the electronic medical record. ACE = angiotensin converting enzyme; ARB = angiotensin receptor blockers.

9 Percent mortality risk based on age, sex, diagnosis, COPS2, LAPS2, and care directive using a predictive model described in text and in citation 22.

10 See text for description of how end of life care directives are captured in the electronic medical record.

11 ICU = intensive care unit. *Direct admit* means that the first hospital unit in which a patient stayed was the ICU; *transfer* refers to those patients transferred to the ICU from another unit in the hospital

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **DESCRIPTION OF STUDY COHORT (PROPENSITY & FACILITY MATCH)** | |  | |  |
|  |  | **Patients initially managed using** | | **P1** |
|  | **All Patients** | **AMI order set2** | **A la carte2 orders** |  |
|  | N=4,012 | N=2,006 | N=2,006 |  |
| **Age in years median(mean ± SD3)** | 71 ( 69.8 ± 13.7) | 71 ( 69.8 ± 13.6) | 70 ( 69.7 ± 13.7) | 0.9236 |
| **Age (% > 65 years)** | 2,480 ( 61.8%) | 1,233 ( 61.5%) | 1,247 ( 62.2%) | 0.6492 |
| **Sex (% male)** | 2,466 ( 61.5%) | 1,243 ( 62.0%) | 1,223 ( 61.0%) | 0.5165 |
| **STEMI4 (% with)** | 281 ( 7.0%) | 135 ( 6.7%) | 146 ( 7.3%) | 0.4962 |
| **Troponin I (% missing)** | 199 ( 4.96%) | 65 ( 3.2%) | 134 ( 6.7%) | <0.0001 |
| **Troponin I median(mean ± SD)** | 0.42 ( 2.9 ± 9.0) | 0.59 ( 3.1 ± 8.5) | 0.30 ( 2.7 ± 9.4) | 0.139 |
| **Charlson Score5 median(mean ± SD)** | 2.0 ( 2.8 ± 1.6) | 2.0 ( 2.8 ± 1.6) | 3.0 ( 2.8 ± 1.6) | 0.6971 |
| **COPS26 median(mean ± SD)** | 21.0 ( 35.6 ± 34.6) | 21.0 ( 35.8 ± 34.4) | 18.0 ( 35.4 ± 34.9) | 0.6766 |
| **LAPS27 (median, mean ± SD)** | 26.0 ( 40.3 ± 47.1) | 28.0 ( 39.9 ± 46.1) | 24.0 ( 40.7 ± 48.1) | 0.5752 |
| **Length of stay in ED (hours) (median, mean ± SD)** | 5.7 ( 5.7 ± 2.9) | 5.7 ( 5.8 ± 2.7) | 5.7 ( 5.7 ± 3.0) | 0.1602 |
| **Patients receiving aspirin within 24 hours8** | 3,846 ( 95.9%) | 1,967 ( 98.1%) | 1,879 ( 93.7%) | <0.0001 |
| **Patients receiving anticoagulation therapy8** | 3,120 ( 77.8%) | 1,569 ( 78.2%) | 1,551 ( 77.3%) | 0.4943 |
| **Patients receiving beta blockers8** | 3,426 ( 85.4%) | 1,787 ( 89.1%) | 1,639 ( 81.7%) | <0.0001 |
| **Patients receiving ACE inhibitors or ARBs8** | 2,386 ( 59.5%) | 1,322 ( 65.9%) | 1,064 ( 53.0%) | <0.0001 |
| **Patients receiving statins8** | 3,592 ( 89.5%) | 1,880 ( 93.7%) | 1,712 ( 85.3%) | <0.0001 |
| **Patient received 1 or more therapies** | 3,996 (99.6%) | 2,006 (100.0%) | 1,990 (99.2%) | <0.0001 |
| **Patient received 2 or more therapies** | 3,931 (98.0%) | 1,997 (99.6%) | 1,934 (96.4%) | <0.0001 |
| **Patient received 3 or more therapies** | 3,730 (93.0%) | 1,940 (96.7%) | 1790 (89.2%) | <0.0001 |
| **Patient received 4 or more therapies** | 3,065 (76.4%) | 1,654 (82.5%) | 1,411 (70.3%) | <0.0001 |
| **Patient received all 5 therapies** | 1,648 (41.1%) | 928 (46.3%) | 720 (35.9%) | <0.0001 |
| **Predicted mortality risk(%)9(median,mean ±SD)** | 1.1 ( 4.3 ± 9.6) | 1.1 ( 3.7 ± 8.1) | 1.2 ( 4.8 ± 10.8) | 0.0001 |
| **Full code at time of hospital entry10 (%)** | 3,488 ( 86.9%) | 1,746 ( 87.0%) | 1,742 ( 86.8%) | 0.8513 |
| **Admitted to ICU11 (%)** |  |  |  |  |
| **Direct admit (%)** | 1,003 ( 25.0%) | 539 ( 26.9%) | 464 ( 23.1%) | 0.0062 |
| **Unplanned Transfer (%)** | 263 ( 6.6%) | 141 ( 7.0%) | 122 ( 6.08%) | 0.2255 |
| **Ever (%)** | 1,710 ( 42.6%) | 822 ( 41.0%) | 888 ( 44.3%) | 0.0351 |
| **Length of stay (hours) (median, mean ± SD)** | 69.8 ( 115.1 ± 154.7) | 69.5 ( 114.7 ± 159.3) | 70.1 ( 115.4 ± 150.0) | 0.895 |
| **Inpatient mortality (%)** | 216 ( 5.4%) | 90 ( 4.5%) | 126 ( 6.3%) | 0.0118 |
| **30 day mortality (%)** | 311 ( 7.8%) | 143 ( 7.1%) | 168 ( 8.4%) | 0.1399 |
| **All cause rehospitalization within 30 days (%)** | 712 ( 17.8%) | 359 ( 17.9%) | 353 ( 17.6%) | 0.8042 |
| **Cardiac cath procedure referral timing** |  |  |  |  |
| **1 day pre adm to disch** | 2,171 ( 54.1%) | 1,106 ( 55.1%) | 1,065 ( 53.1%) | 0.5686 |
| **2 days pre adm or earlier** | 150 ( 3.7%) | 73 ( 3.6%) | 77 ( 3.8%) |  |
| **After discharge** | 175 ( 4.4%) | 82 ( 4.1%) | 93 ( 4.6%) |  |
| **No referral** | 1,516 ( 37.8%) | 745 ( 37.1%) | 771 ( 38.4%) |  |

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11 ICU = intensive care unit. *Direct admit* means that the first hospital unit in which a patient stayed was the ICU; *transfer* refers to those patients transferred to the ICU from another unit in the hospital

**FIGURE: DISTRIBUTION OF PROPENSITY SCORES**

FIGURE 1:

Distribution of propensity scores (see text for details of how these were assigned) based on use or non-use of the acute myocardial infarction order set. The ***x*** axis shows the propensity score range, while the ***y*** axis shows the percent of patients within a given propensity score range. The distribution of scores for patients whose first set of orders employed the order set is shown on the top panel, while the bottom panel shows the distribution in patients in whom the first set of orders did not use the order set.

**APPENDIX 5: RELATIVE RISK OF PROCESS OR OUTCOME FOR PATIENTS RECEIVING AMI-OS**

The table below show outcomes other than inpatient death (30-day mortality, LOS, and readmission) and their robustness under different statistical approaches. The table shows the relationship between AMI-OS use and evidence-based therapies and outcomes of care based on different statistical methods. Use of the AMI-OS was strongly associated with both receiving individual therapies as well as receiving multiple therapies. The table also shows the impact of the AMI-OS on mortality and rehospitalization using the two different propensity score approaches (inverse probability weighting and matched analyses) with and without incorporation of the 5 therapies in the risk adjustment. As with the logistic regression on inpatient mortality analysis above, the analyses without the therapies shows that theuse of the AMI-OS was significantly protective with respect to mortality but not significant with respect to total hospital LOS or rehospitalization. With respect to mortality, the magnitude of this protective effect decreased after multivariate adjustment, and lost statistical significance when the 5 process variables were incorporated into the risk adjustment mode. For example, with respect to inpatient mortality, the unadjusted relative risk for use of the AMI-OS was 0.54 (95% CI 0.43-0.68), which was lower than that obtained using inverse probability weighting (0.70, 95% CI 0.55-0.87) or propensity risk score matching (0.69, 95% CI 0.54-0.89), and lost statistical significance when the process variables were included.

**Adjusted Odds Ratio or Mean Length of Stay Ratio in Study Patients – Patients With ST-Segment Elevation MI Excluded**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Outcome** | **Order Set1** | **Three Therapies2** | **Four Therapies2** | **Five Therapies2** |
| Average Treatment Effect (ATE)3 | | | | |
| Inpatient Mortality | 0.63 (0.48, 0.84) | 0.58 (0.37, 0.88) | 0.35 (0.23, 0.52) | 0.18 (0.11, 0.28) |
| 30-Day Mortality | 0.70 (0.55, 0.88) | 0.65 (0.45, 0.95) | 0.36 (0.25, 0.52) | 0.23 (0.15, 0.34) |
| Readmission | 0.99 (0.85, 1.14) | 1.25 (0.89, 1.76) | 1.22 (0.89, 1.67) | 1.32 (0.96, 1.82) |
| LOS (ratio of the geometric means) | 0.90 (0.86, 0.94) | 1.14 (1.01, 1.28) | 1.15 (1.03, 1.28) | 1.11 (0.99, 1.24) |
| Average Treatment Effect on the Treated (ATT)4 | | | | |
| Inpatient Mortality | 0.60 (0.44, 0.82) | 0.24 (0.09, 0.66) | 0.14 (0.05, 0.39) | 0.09 (0.03, 0.24) |
| 30-Day Mortality | 0.72 (0.55, 0.93) | 0.38 (0.17, 0.85) | 0.19 (0.09, 0.40) | 0.13 (0.06, 0.28) |
| Readmission | 1.03 (0.87, 1.22) | 1.03 (0.60, 1.77) | 1.07 (0.65, 1.76) | 1.13 (0.69, 1.85) |
| LOS (ratio of the geometric means)5 | 0.89 (0.84, 0.95) | 1.26 (1.08, 1.46) | 1.22 (1.06, 1.40) | 1.09 (0.95, 1.25) |

1Refers to comparison in which the reference group consists of patients who were not treated using the acute myocardial infarction order set. 2Refers to comparison in which the reference group consists of patients who received 2 or less of the 5 recommended therapies. 3See text for description of ATE methodology. 4See text for description of ATT and matched pair adjustment methodology. 5See text for details on how we modeled LOS.